

BALB/c-hIL1B

Strain Name: BALB/cJGpt-*Il1b*^{em1Cin(hIL1B)}/Gpt

Strain Type: Knock-in

Strain Number: T053555

Background: BALB/cJGpt

Description

IL1B is a member of the interleukin 1 family of cytokines, and it's a central mediator of innate immunity and inflammation. As a key pro-inflammatory factor, IL1B is involved in a variety of autoimmune inflammatory responses and a variety of cellular activities, including cell proliferation, differentiation and apoptosis, and is widely associated with the development of inflammatory diseases^[1].

Numerous studies have shown that upon exogenous or endogenous stimulation, the NALP3 inflammasome is capable of activating caspase 1 (caspase 1), and pro-IL1B is processed and released from innate immune cells to biologically active IL1B by a mechanism involving caspase 1^[2, 3]. When IL1B is overexpressed, it can lead to rheumatoid arthritis, neuropathic pain, inflammatory bowel disease, type 2 diabetes, Alzheimer's disease and autoimmune diseases, etc. It was reported that IL1B secretion was elevated in malignant tumors such as lung adenocarcinoma cells and colon cancer, and inhibiting the expression of IL1B reduces the development of cancer cells, proving that blocking IL1B can be used to treat cancer caused by inflammation^[4-6]. At present, the development of inhibitors targeting IL-1B to alleviate tissue damage and carcinogenesis caused by inflammatory responses has received more and more attention.

GemPharmatech used gene editing technology to replace the whole coding sequence of IL1B in BALB/c mice with the human counterpart, and developed BALB/c-hIL1B humanized model. This model has fully humanized IL-1B and is an ideal humanized model for chronic inflammation and malignant tumor treatment research.

Strategy

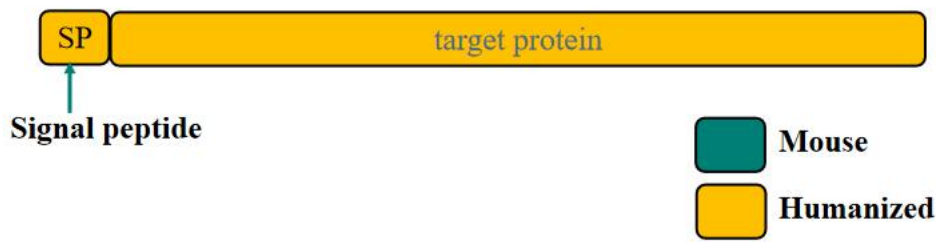


Fig.1 Schematic diagram of BALB/c-hIL1B model strategy.

Applications

- 1.Evaluation of the efficacy of human IL-1B inhibitor
- 2.Anti-inflammation drug research and development
- 3.Anti-cancer drug research and development
- 4.Research on autoimmune diseases

Data support

1. Detection of IL1B expression

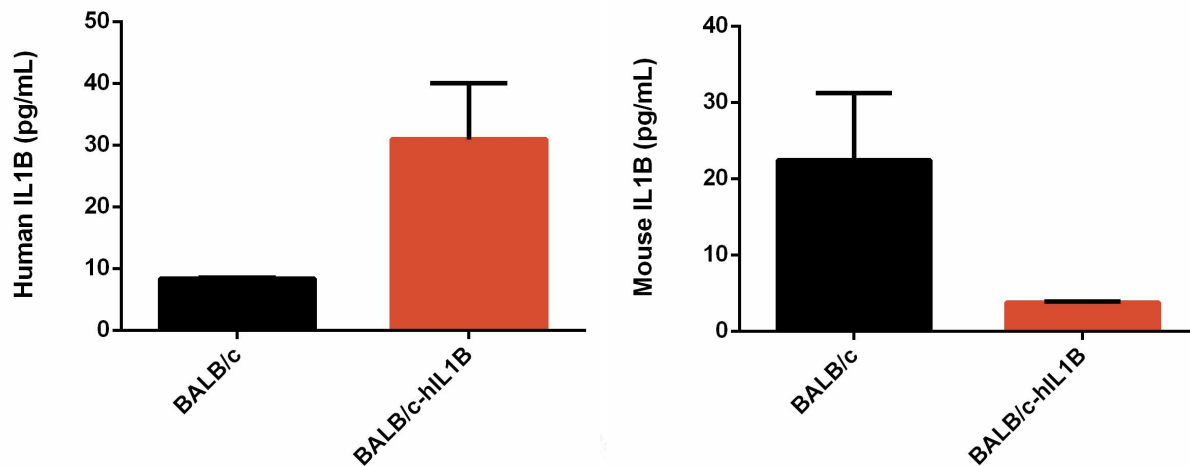


Fig 2. Detection of hIL1B expression on BALB/c-hIL1B mice.

Mice were stimulated with LPS through intraperitoneal injection and analyzed for IL1B expression. The expression of human IL1B protein can be detected in homozygous BALB/c-hIL1B but not BALB/c wild type mice.

2. Analysis of blood immune cell subpopulations in BALB/c-hIL1B mice

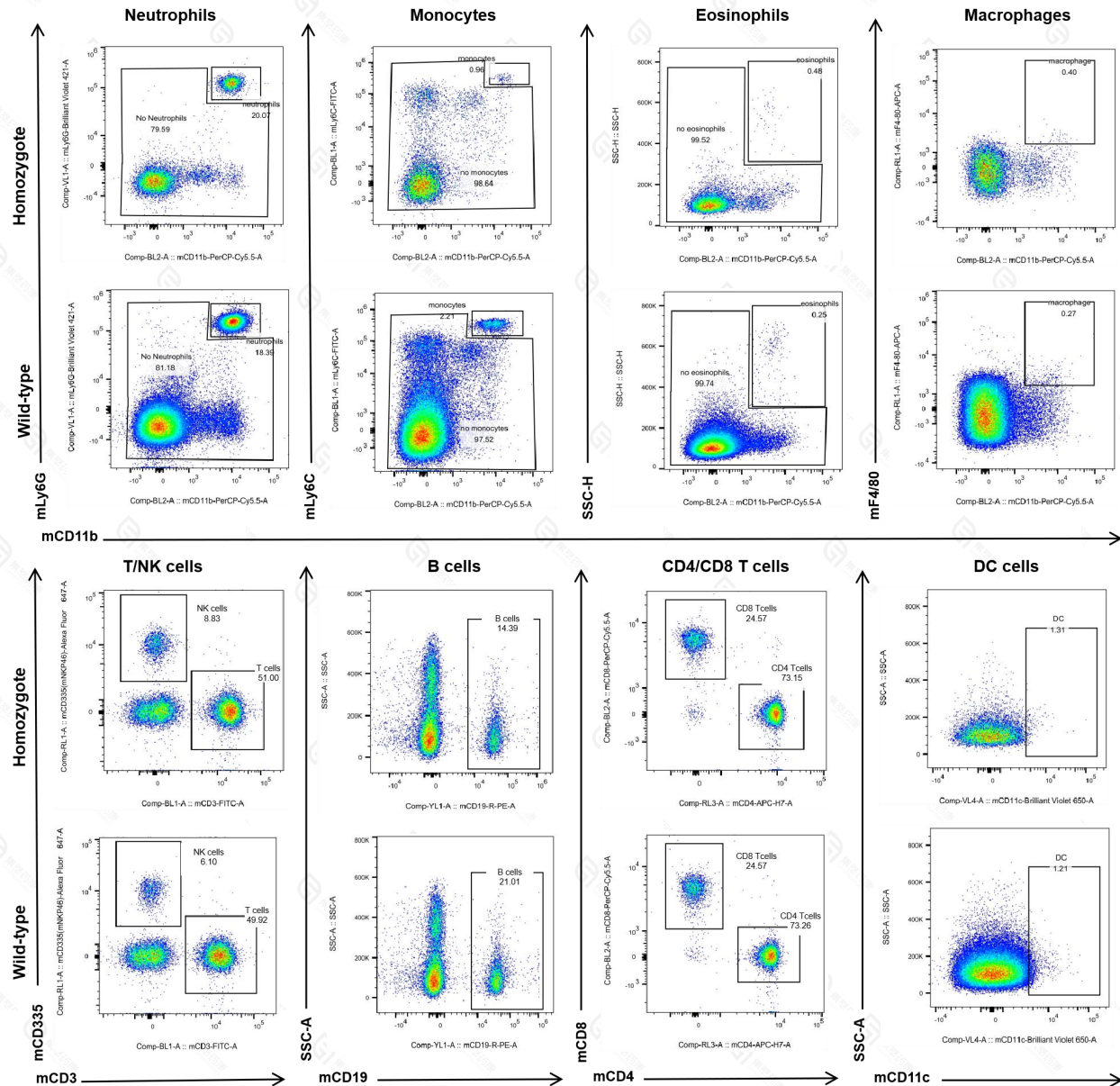


Fig 3. Analysis of blood immune subpopulation in BALB/c and BALB/c-hiL1B.

Blood was taken from BALB/c and BALB/c-hiL1B mice for flow cytometric analysis to assess immune cell subpopulations. As shown in Figure 3, the percentages of T cells, NK cells, B cells, neutrophils, monocytes, macrophages and dendritic cells in BALB/c-hiL1B mice were similar to those in BALB/c, indicating that the replacement of mIL1B by hiL1B did not alter the development, differentiation, and distribution of these cells in blood.

3. Analysis of spleen immune cell subpopulations in BALB/c-hiL1B mice

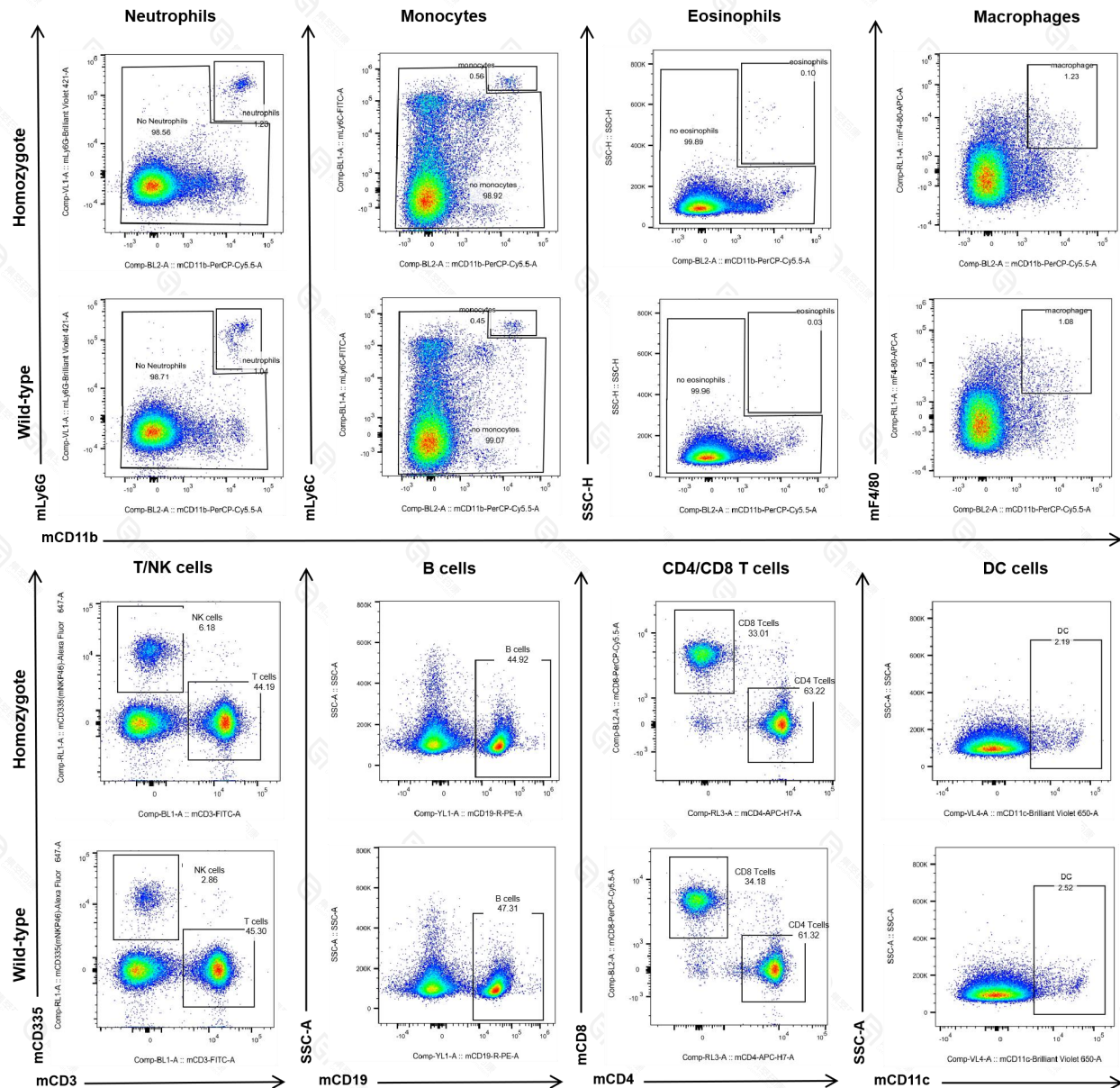


Fig 4. Analysis of spleen immune subpopulations in BALB/c and BALB/c-hl1B.

Splenocytes were taken from BALB/c and BALB/c-hl1B mice for flow cytometric analysis to assess immune cell subpopulations. As shown in Figure 4, the percentages of T cells, NK cells, B cells, neutrophils, monocytes, macrophages and dendritic cells in BALB/c-hl1B mice were similar to those in BALB/c, indicating that the replacement of mIL1B by hl1B did not alter the development, differentiation, and distribution of these cells in spleen.

References

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2. Gabay C, Lamacchia C, Palmer G. IL-1 pathways in inflammation and human diseases. *Nat Rev Rheumatol*. 2010 Apr;6(4):232-41.
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6. Dinarello CA, Simon A, van der Meer JW. Treating inflammation by blocking interleukin-1 in a broad spectrum of diseases. *Nat Rev Drug Discov*. 2012 Aug;11(8):633-52.