B6-hCD47/hSIRPA

Strain Name： B6/JGpt-*CD47*$^{em1Cin(hCD47)}$*Sirpa*$^{em1Cin(hSIRPA)}$/Gpt
Strain Type： Knock-in
Strain Number： T037007
Background： C57BL/6JGpt

Description

CD47, also known as integrin-associated protein (IAP), is widely expressed on the surface of cells. CD47 can interact with inhibitory receptor signaling protein alpha (SIRPA), thrombospondin (TSP1), and integrins mediating a series of reactions such as apoptosis, proliferation, and immunity [1, 2]. Studies have confirmed that CD47 molecules are over-expressed in many malignant tumors, such as acute myeloid leukemia (AML), B-cell and T-cell acute leukemia, non-Hodgkin's lymphoma, and their expression level negatively correlated with the prognosis of the disease. Tumor cells can escape the immune surveillance of macrophages through the CD47-SIRPa signaling pathway. Therefore, blocking the binding of CD47 to SIRPA by CD47 antibody can activate the phagocytosis of macrophage and the antigen presentation of DC cells. CD47 can combine with other immunotherapies to inhibit tumor growth [3,4].

Blocking CD47-SIRPA interactions has been shown to promote the destruction of cancer cells by phagocytes, including macrophages and neutrophils. Furthermore, there is growing evidence that targeting of the CD47-SIRPA axis may also promote antigen-presenting cell function and thereby stimulate adaptive T cell-mediated anti-cancer immunity [5-8]. These identify the CD47-SIRPA axis as a promising innate immune checkpoint in cancer.

The B6-hCD47/hSIRPA was created at GemPharmatech by crossing the B6-hCD47 strain with the B6-hSIRPA strain. This model completely preserves the intracellular portion of mouse CD47 and SIRPA protein, ensuring normal intracellular signal transduction. This strain successfully expressed human CD47 and human SIRPA. B6-hCD47/hSIRPA is an ideal animal model for evaluating the efficacy and safety of human CD47 and human SIRPA antibodies.

Strategy

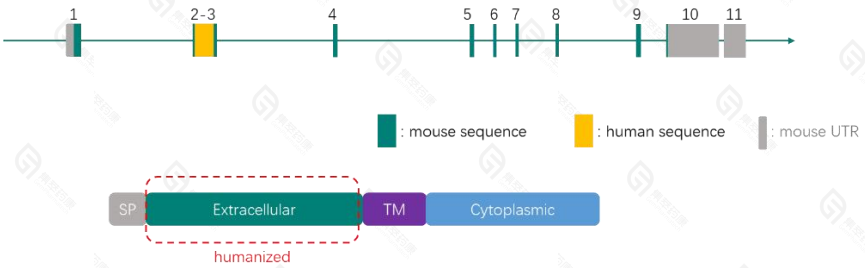

Fig 1. Schematic diagram of CD47 humanization strategy in B6-hCD47/hSIRPA mice.

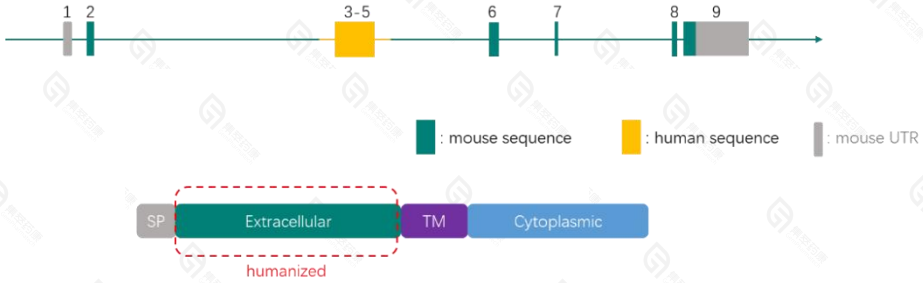

Fig 2. Schematic diagram of SIRPA humanization strategy in B6-hCD47/hSIRPA mice.

Applications

1. Screening for human CD47 or human SIRPA related drugs
2. Efficacy and safety evaluation of human CD47 or human SIRPA related drugs
3. Immune system related research

Data support

1. Detection of CD47 and SIRPA expression

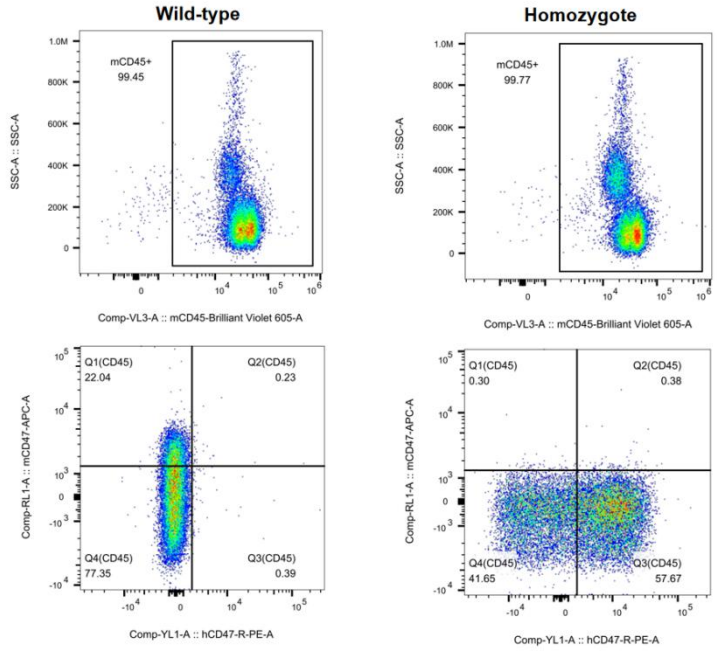

Fig 3. Detection of CD47 expression in peripheral blood lymphocytes on B6-hCD47/hSIRPA mice. Peripheral blood lymphocytes were collected from wild-type (6-7 weeks) and B6-hCD47/hSIRPA mice (6-7 weeks) and analyzed for CD47 expression with flow cytometry. The human CD47 expression of CD45+ cells in homozygous B6-hCD47/hSIRPA is comparable to the mouse CD47 counterpart in wild-type B6 mice.

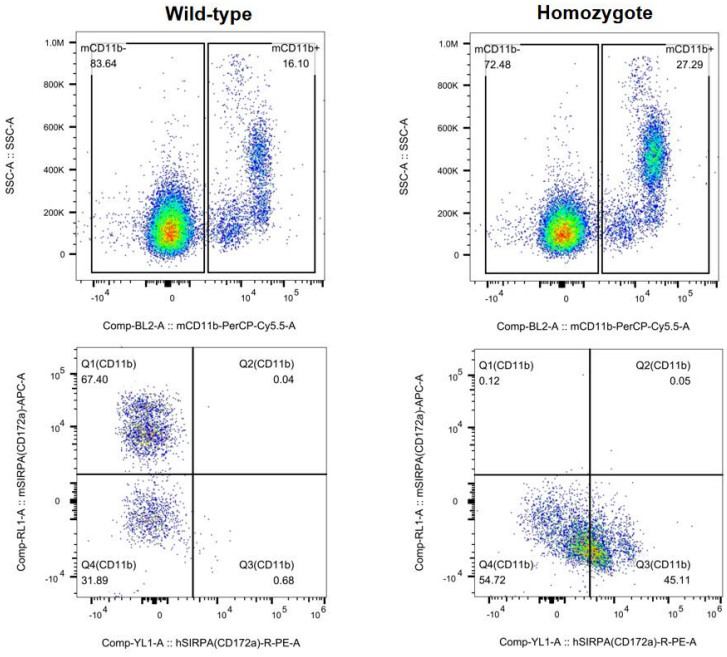

Fig 4. Detection of SIRPA expression in peripheral blood lymphocytes on B6-hCD47/hSIRPA mice. Peripheral blood lymphocytes were collected from wild-type (6-7 weeks) and B6-hCD47/hSIRPA mice (6-7 weeks) and analyzed for SIRPA expression with flow cytometry. The human SIRPA expression of

mCD11b+ cells in homozygous B6-hCD47/hSIRPA is comparable to the mouse SIRPA counterpart in wild-type B6 mice.

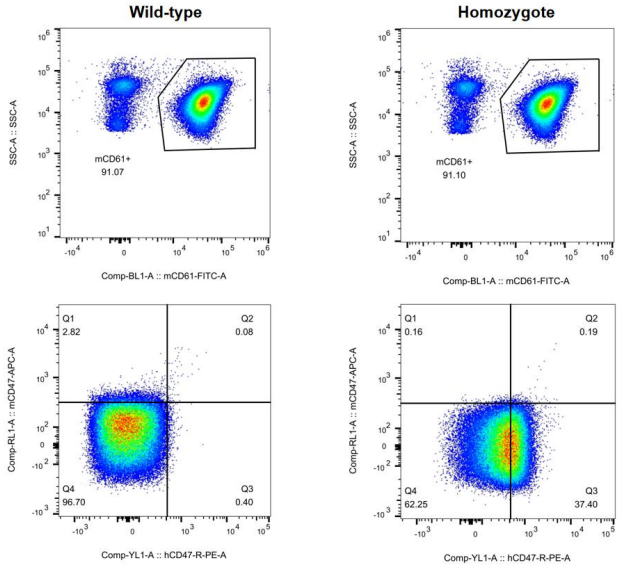

Fig 5. Detection of CD47 expression in peripheral blood lymphocytes on B6-hCD47/hSIRPA mice. Peripheral blood lymphocytes were collected from wild-type (6-7 weeks) and B6-hCD47/hSIRPA mice (6-7 weeks) and analyzed for CD47 expression with flow cytometry. The surface of platelets (mCD61+) on B6-hCD47/hSIRPA mice expressed hCD47.

2. Leukocyte subpopulation analysis

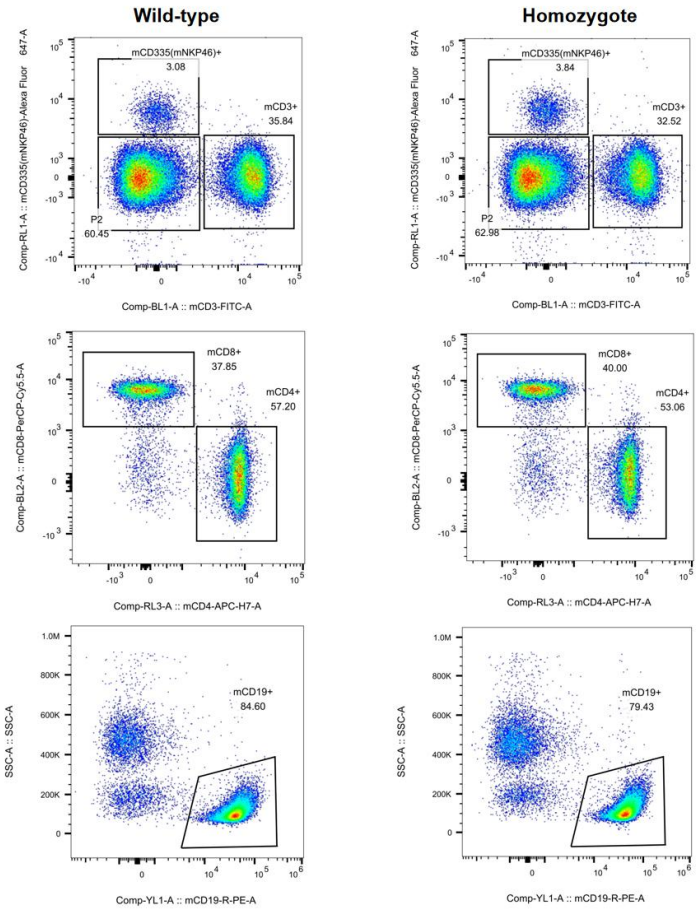

Fig 6. Analysis of leukocyte subpopulation in splenocytes on B6-hCD47/hSIRPA mice. Splenocytes were collected from wild-type (6-7 weeks) and B6-hCD47/hSIRPA mice (6-7 weeks) and analyzed for leukocyte subpopulation with flow cytometry. The ratio of T cells (mCD3+, mCD4+ and mCD8+), B cells (mCD19+) and NK cells (mCD335+) in the spleen of B6-hCD47/hSIRPA mice were similar to that of wild-type B6 mice.

References

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