BALB/c-hNECTIN-4

Strain Name： BALB/cJGpt-*Nectin4*$^{em1Cin(hNECTIN4)}$/Gpt
Strain Type： Knock-in
Strain Number： T056430
Background： BALB/c

Description

NECTIN4(nectin cell adhesion molecule 4), also known as PVRL4(Poliovirus receptor-related 4), is a cellular adhesion molecule involved in Ca^{2+} independent cellular adhesion[1,2]. It is mainly expressed in normal embryonic and fetal tissues, but expressed at a very low level in adult healthy tissues. NECTIN4 is a single-pass type I membrane protein contains two immunoglobulin-like (Ig-like) C2-type domains and one Ig-like V-type domain. The soluble form is produced by proteolytic cleavage at the cell surface by the metalloproteinase ADAM17/TACE. The secreted form is found in both breast tumor cell lines and breast tumor patients.

NECTIN4 is particularly overexpressed in a number of tumor types, including breast, lung, skin, urothelial, colorectal, pancreatic and ovarian cancer[3]. Mutations in this gene are the cause of ectodermal dysplasia-syndactyly syndrome type 1, an autosomal recessive disorder[4]. NECTIN4 has been used as a potential target in antibody-drug conjugate (ADC) development.

Gempharmatech developed BALB/c-hNECTIN-4 humanized model by replacing the signal peptide and extracellular domain of NECTIN4 in BALB/c mice with the human corresponding fragment to ensure endogenous intracellular signaling functional. This strain will facilitate cancer related research and drug development.

Strategy

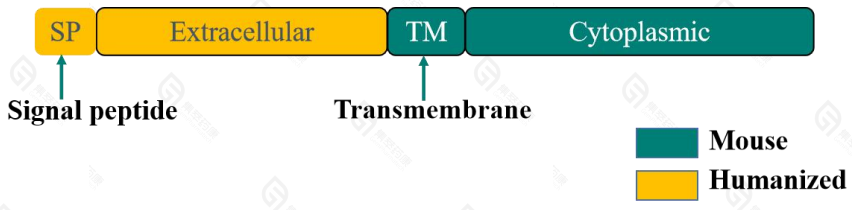

Fig 1. Schematic diagram of NECTIN4 humanization strategy on BALB/c-hNECTIN-4 mice.

Applications

1.Screening, preclinical efficacy evaluation and safety evaluation of human NECTIN4 blockades

2. Research on anti-tumor

Data support

1. Expression of NECTIN4/PVRL4

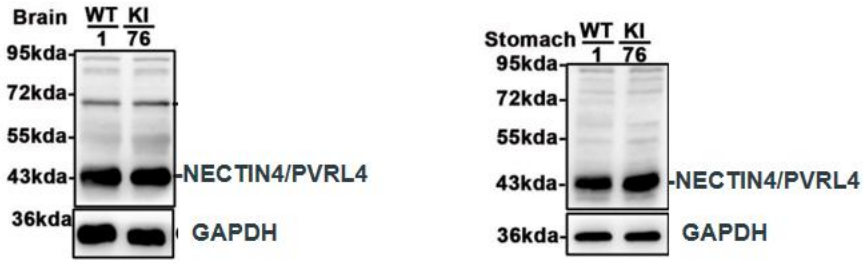

Fig 2. Expression of NECTIN4/PVRL4 in BALB/c-hNECTIN-4 homozygous mice.

The cross-reaction antibody was used to detect the mouse endogenous and humanized NECTIN4 expression. In BALB/c-hNECTIN-4 homozygous mice, human NECTIN4 /PVRL4 was expressed in brain tissue and stomach tissue.

2. Analysis immune cell subpopulations in BALB/c-hNECTIN-4 mice

2.1Analysis of blood immune cell subpopulations

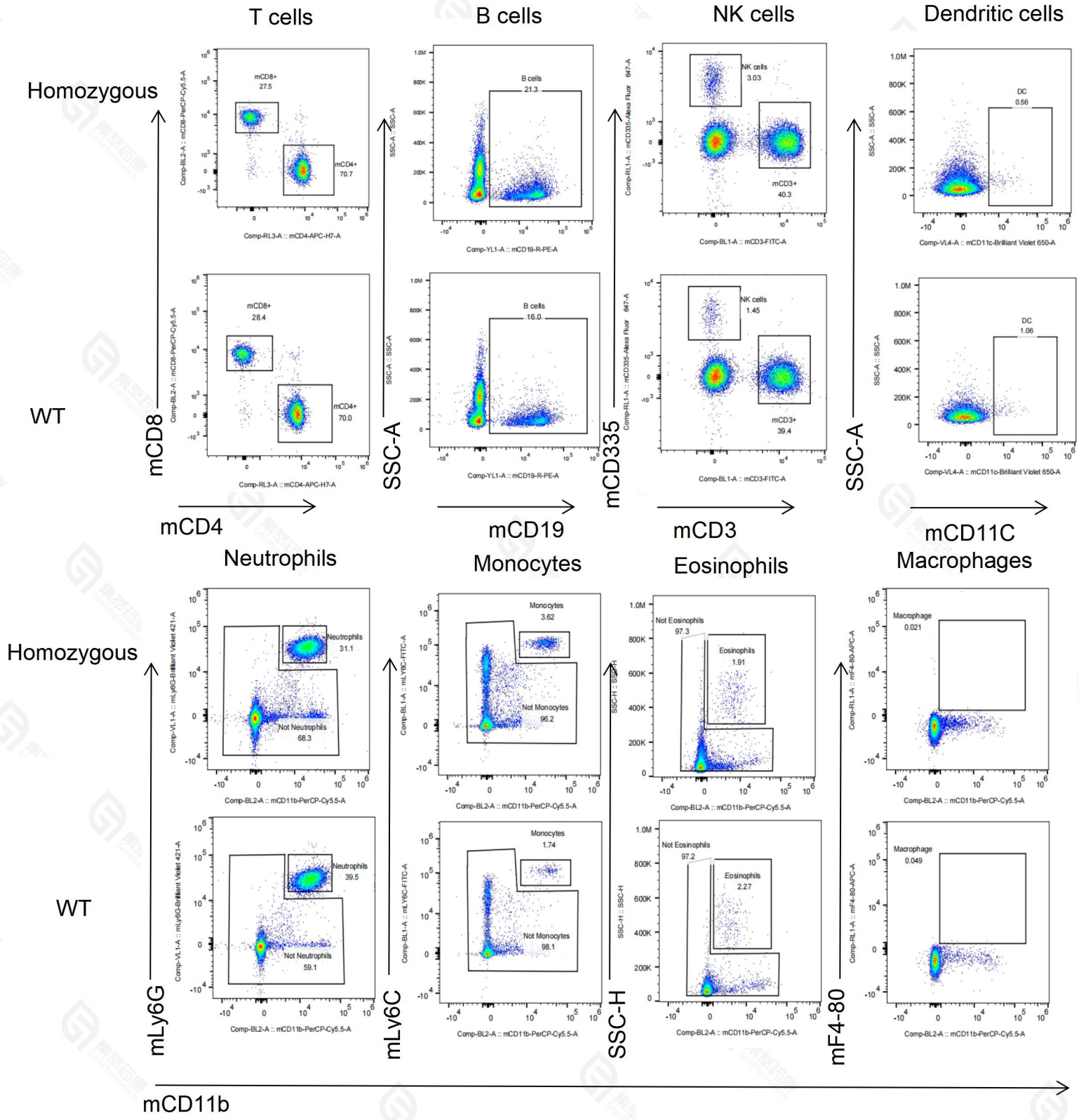

Fig 3. Immune cell subpopulations analysis in BALB/c and BALB/c-hNECTIN-4

Blood was taken from BALB/c and BALB/c-hNECTIN-4 mice for flow cytometric analysis to assess immune subpopulations. As shown in Figure 3, the percentages of T cells, B cells,NK cells,dendritic cells,neutrophils, monocytes, eosinophils, macrophages in BALB/c-hNECTIN-4 mice were similar to those in BALB/c, indicating that the replacement of mNECTIN-4 by hNECTIN-4 did not alter the development, differentiation, and distribution of these cells in blood.

2.2Analysis of spleen immune cell subpopulations

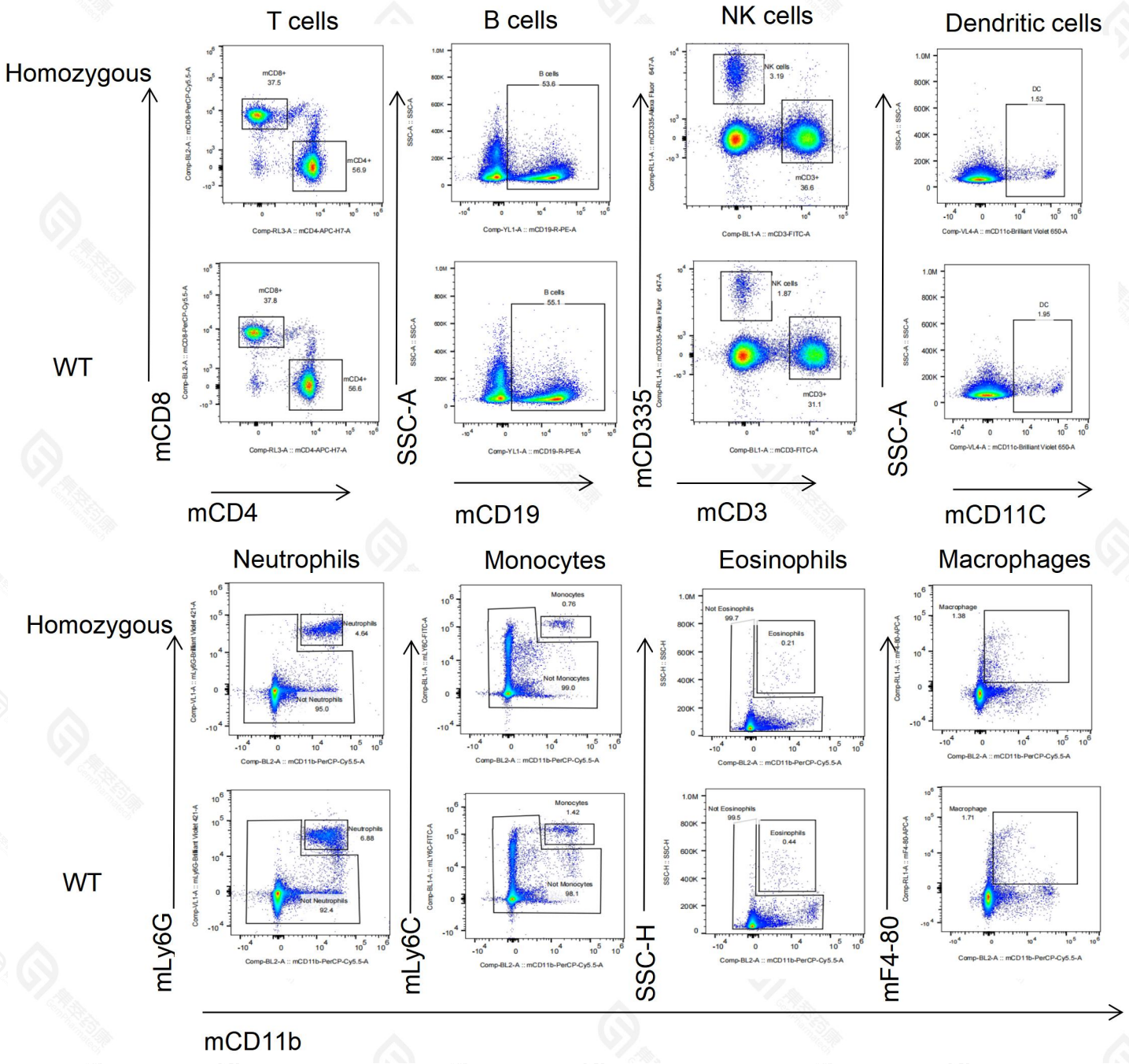

Fig 4. Leukocyte subpopulations analysis in spleen of BALB/c and BALB/c-hNECTIN-4

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

References

1. Takai Y., et al. "Nectins and nectin-like molecules: roles in cell adhesion, migration, and polarization. "Cancer Sci. 2003 Aug;94(8):655-67.
2.Fuchs A., et al. "The role of NK cell recognition of nectin and nectin-like proteins in tumor immunosurveillance. "Semin Cancer Biol. 2006 Oct;16(5):359-66.
3. Liu Y., et al. "Role of Nectin-4 protein in cancer (Review). "Int J Oncol. 2021 Nov;59(5):93.
4. Brancati F., et al. "Mutations in PVRL4, encoding cell adhesion molecule nectin-4, cause ectodermal dysplasia-syndactyly syndrome. " Am J Hum Genet. 2010 Aug 13;87(2):265-73.