B6-hCD200R1

Strain Name: C57BL/6JGpt-*CD200R1*$^{em1Cin(hCD200R1)}$/Gpt
Strain Type: Knock-in
Strain Number: T054639
Background: C57BL/6JGpt

Description

CD200R1 (CD200 receptor 1), which encodes the receptor of CD200, mainly expresses on the surface of myeloid cells. CD200R1 is reported to inhibit immune responses and regulate myeloid function by binding CD200 [1]. Metabolic regulation targeting CD200R1 is of great significance in atherosclerosis and related diseases.

Innate immunity activation is one of the important causes of atherosclerotic diseases [2]. Immune checkpoints have been shown to play an important role in the formation of atherosclerosis. They can activate receptor-ligand pairs, thereby controlling the activation of T cells and antigen presenting cells and regulating the immune response. As an immunomodulation checkpoint [3], CD200-CD200R1 regulates the process of atherosclerosis. It has been reported that the CD200-CD200R1 pathway mediates cell-to-cell interactions, thereby preventing STAT1 activation in myeloid cells, ultimately reducing the progression of atherosclerotic plaques and inhibiting the formation of inflammation and necrosis [4]. Therefore, targeting CD200R1 may be an effective strategy for the treatment of atherosclerosis diseases.

Gempharmatech used CRISPR/Cas9 system to introduce the CDS and 3' UTR region of human CD200R1 gene into mice, and successfully constructed the CD200R1 humanized mouse model, B6-hCD200R1 (T054639). B6-hCD200R1 can be used to evaluate the efficacy of clinical drugs targeting CD200R1 for the treatment of atherosclerosis.

Strategy

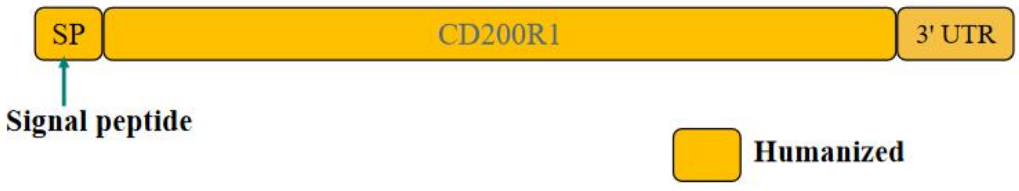

Fig.1 Schematic diagram of B6-hCD200R1 model stratery.

Applications

1. Screening and efficacy evaluation of drugs related to human atherosclerosis
2. Targeting CD200R1 in atherogenesis related mechanisms

Data support

1. Detection of hCD200R1 mRNA expression

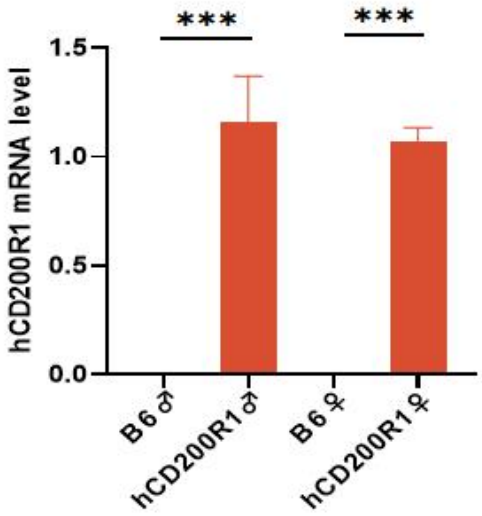

Fig 2. Human CD200R1 was expressed in hCD200R1 mice but not expressed in B6 wildtype mice

The mRNA expression level of human CD200R1 gene was detected by RT-qPCR using primers that specifically recognized human CD200R1.The spleen of B6 mice and hCD200R1 mice were used in the detection.The mice were 14 weeks old. (n=3；3♂, 3♀; data were showed as Mean±SEM, ***denoted p<0.001 vs B6)

2. Detection of mCd200r1 mRNA expression

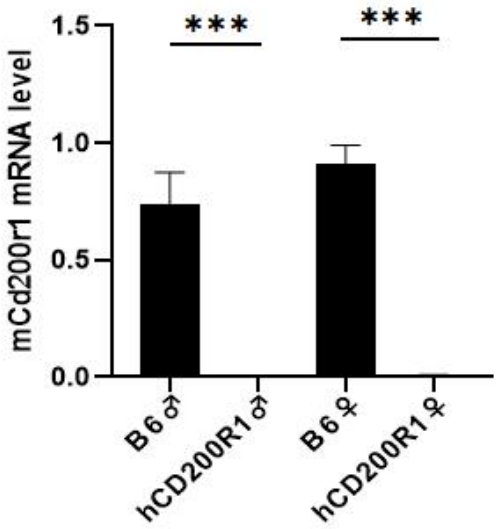

Fig 3. Mouse Cd200r1 was expressed in B6 wildtype mice but not expressed in hCD200R1 mice
The mRNA expression level of mouse Cd200r1 gene was detected by RT-qPCR using primers that specifically recognized mouse Cd200r1.The spleen of B6 background mice and hCD200R1 mice were used in the detection. The mice were 14 weeks old. (n=3；3♂, 3♀; data were showed as Mean±SEM, ***denoted p<0.001 vs B6)

3. Detection of B6-hCD200R1 mice body weight

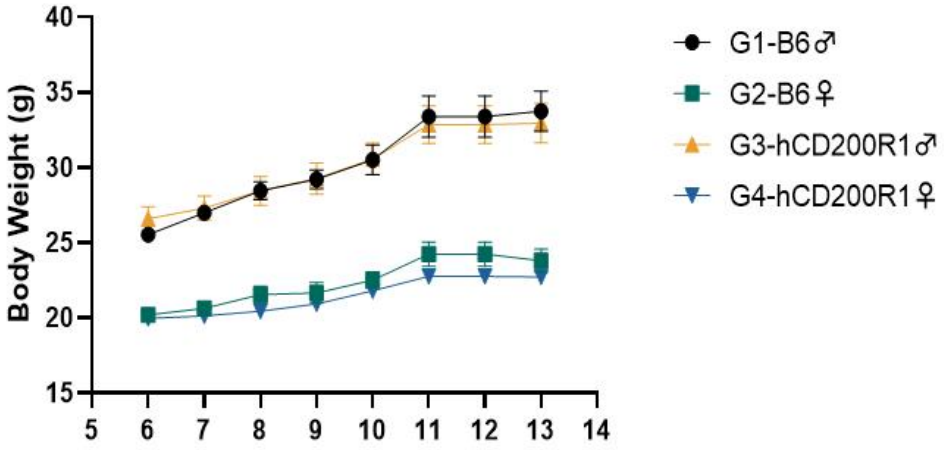

Fig 4. Body weight of B6-hCD200R1 and B6 mice with age
The hCD200R1 mice and B6 mice were started at 5-6 weeks of age, and fed with normal diet. The body weight data were collected weekly (n=5; 5♂, 5♀).Data were collected for 8 weeks. The weight change trend of B6-hCD200R1 and B6 control mice was similar, and the weight of male mice was higher than that of female mice.

4. Detection of blood lipid expression in B6-hCD200R1 mice

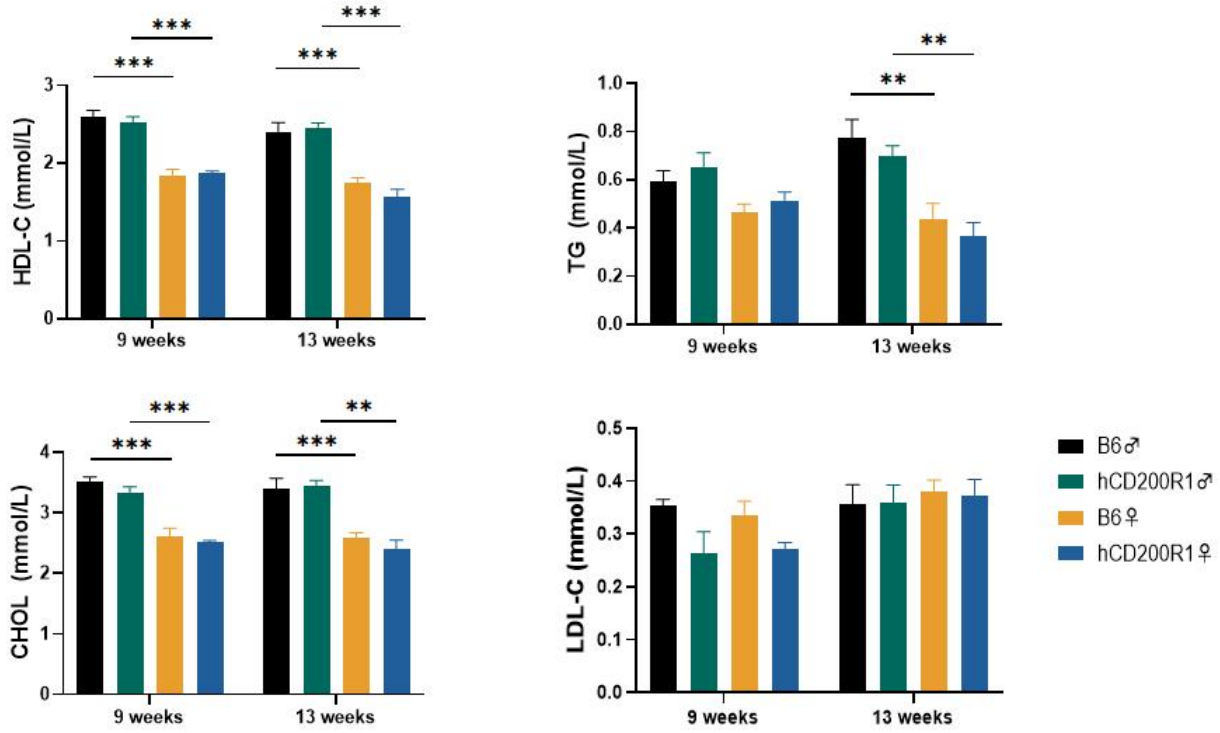

Fig 5. The serum lipid expression level of B6-hCD200R1 was similar to that of B6 mice

The plasma lipid levels of B6 mice (n=5; 5♂, 5♀)and hCD200R1 mice (n=5; 5♂, 5♀)at 9 and 13 weeks of age were detected by blood biochemical analyzer. At 9 weeks of age, the LDL-C level of B6 mice was slightly higher than that of hCD200R1 mice. The TG levels of the hCD200R1 mice were slightly higher than that of B6 mice，but there was no statistical significance. At 13 weeks of age, the serum lipid expression level of B6-hCD200R1 mice was similar to that of B6 mice. (Data were showed as Mean±SEM, **,***denoted p<0.01, p<0.001 vs B6, respectively)

5. Detection of lipid expression level in liver of B6-hCD200R1 mice

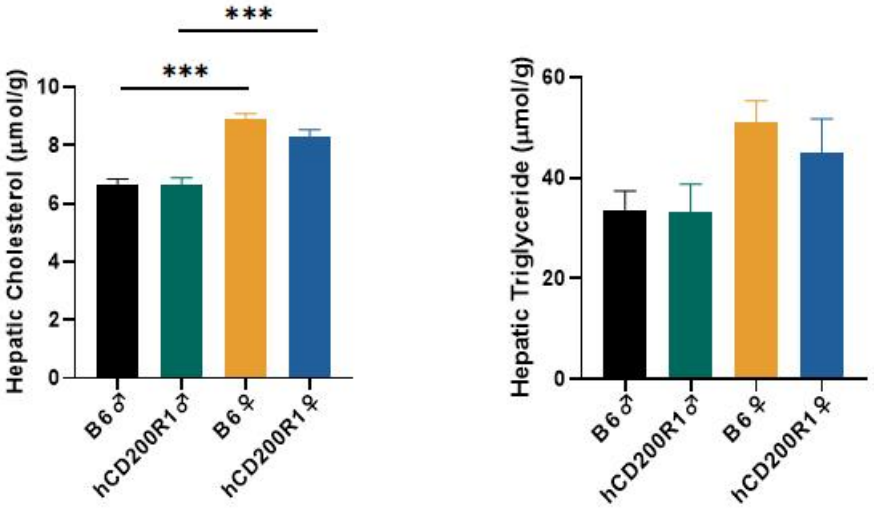

Fig 6. The liver lipid expression level of B6-hCD200R1 was similar to that of B6 mice

Lipid expression levels in liver homogenate supernatant of 13-week-old B6 mice (n=5; 5♂, 5♀)and hCD200R1 mice (n=5; 5♂, 5♀) were detected by blood biochemical assay. The expression level of lipid in the liver of B6-hCD200R1 mice was similar to that of B6 mice, and the expression level of TG and CHOL in male mice was lower than that in female mice. (Data were showed as Mean±SEM, ***denoted p<0.001 vs B6)

References

1. Wright GJ, Cherwinski H, Foster-Cuevas M, Brooke G, Puklavec MJ, Bigler M, Song Y, Jenmalm M, Gorman D, McClanahan T, et al. Characterization of the cd200 receptor family in mice and humans and their interactions with cd200. Journal of immunology. 2003;171:3034-3046.
2. Kusters PJH, Lutgens E, Seijkens TTP. Exploring immune checkpoints as potential therapeutic targets in atherosclerosis. Cardiovascular research. 2018;114:368-377.
3. Wright GJ, Puklavec MJ, Willis AC, Hoek RM, Sedgwick JD, Brown MH, Barclay AN. Lymphoid/neuronal cell surface ox2 glycoprotein recognizes a novel receptor on macrophages implicated in the control of their function. Immunity. 2000;13:233-242.
4. Kassiteridi C, Cole JE, Griseri T, et al. CD200 Limits Monopoiesis and Monocyte Recruitment in Atherosclerosis. Circ Res. 2021;129(2):280-295.