B6-hAPOB-Tg

Strain Name: C57BL/6JGpt-Tg(APOB)184/Gpt
Strain Type: Transgenic(Tg)
Strain Number: T058217
Background: C57BL/6JGpt

Description

APOB encodes apolipoprotein B, which is the main apolipoprotein of chylomicron (CM) and low-density lipoprotein (LDL), and it is also a ligand for LDL receptors[1]. Therefore, metabolic regulation targeting APOB is of great significance in atherosclerosis, hypercholesterolemia and related diseases.

In humans, APOB exists in plasma as two major isomers, apoB-48 and apoB-100[2]. The former is synthesized in the intestine and is necessary for CM production in the small intestine. The latter is synthesized in the liver and is necessary for VLDL production in the liver. And in rodents, unlike humans, about 60% of apoB-100 mRNA is edited into apoB-48 mRNA in the liver. This phenomenon may result in low LDL-C expression in mice[1,3,4] . Recently,increased concentrations of APOB-containing lipoproteins in plasma have been shown to be a key factor for the development of atherosclerosis. Therefore, targeting APOB may be an effective strategy for the treatment of atherosclerosis and hypercholesterolemia related diseases.

Gempharmatech used gene editing technology to introduce the CDS, 5' UTR and 3' UTR region of human APOB gene into mice, and successfully constructed the APOB humanized mouse model, B6-hAPOB-Tg (T058217). B6-hAPOB-Tg can be used to evaluate the efficacy of clinical drugs targeting APOB for the treatment of hypercholesteremia and atherosclerosis.

Strategy

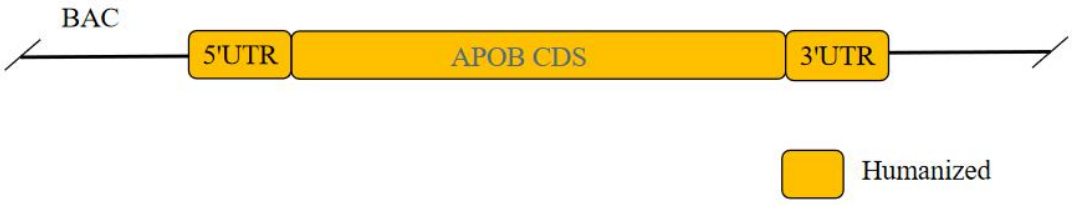

Fig.1 Schematic diagram of B6-hAPOB-Tg model strategy.

Applications

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

Data support

1. Detection of APOB protein expression

Human APOB protein was successfully expressed in hAPOB mice, and the expression of human APOB protein was stable in the N2 and N3 generations without trait segregation.

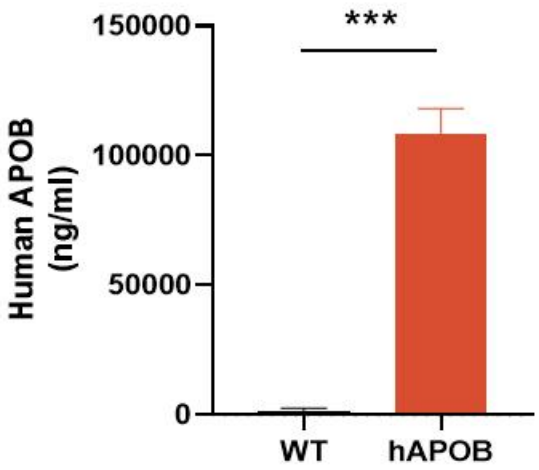

Fig 2. The hAPOB protein was successfully expressed in B6-hAPOB-Tg(N2 generation) mice

The plasma samples from B6 background mice and hAPOB-N2 generation mice were tested by ELISA with a specific human APOB recognition kit. The B6 group consisted of 7-8 weeks old B6 background mice (n=4; 2♂, 2♀); The hAPOB group consisted of 7-8 weeks old hAPOB-N2 generation mice（n=5; 3♂, 2♀)

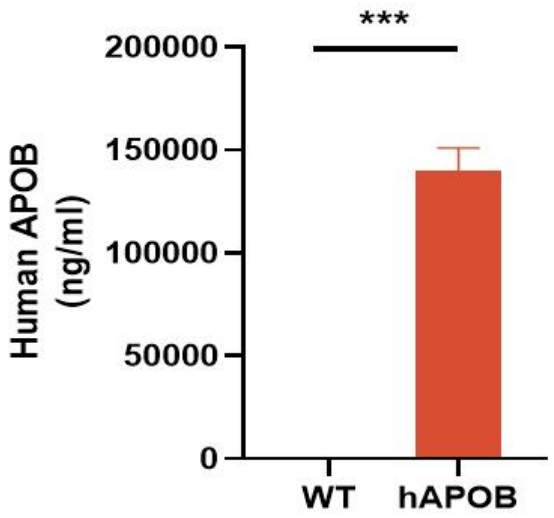

Fig 3. The hAPOB protein was successfully expressed in B6-hAPOB-Tg(N3 generation) mice

The plasma samples from B6 background mice and hAPOB-N3 generation mice were tested by ELISA with a specific human APOB recognition kit. The B6 group consisted of 7-8 weeks old B6 background mice (n=4; 2♂, 2♀); The hAPOB group consisted of 7-8 weeks old hAPOB-N3 generation mice（n=6; 3♂, 3♀).

2. Detection of APOB mRNA expression

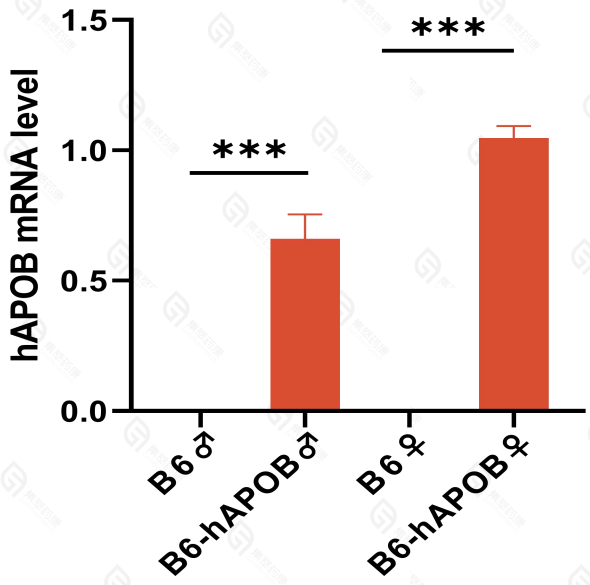

Fig 3. Human APOB was successfully expressed in B6-hAPOB-Tg(N2 generation) mice

The mRNA level of human APOB gene was detected by RT-qPCR in the liver tissues from B6 mice and hAPOB-N2 generation mice. The B6 group consisted of 7-8 weeks old B6 background mice (n=3; 3♂, 3♀); The hAPOB group consisted of 7-8 weeks old hAPOB-N2 generation mice（n=3; 3♂, 3♀).

3. Detection of APOB blood lipid expression

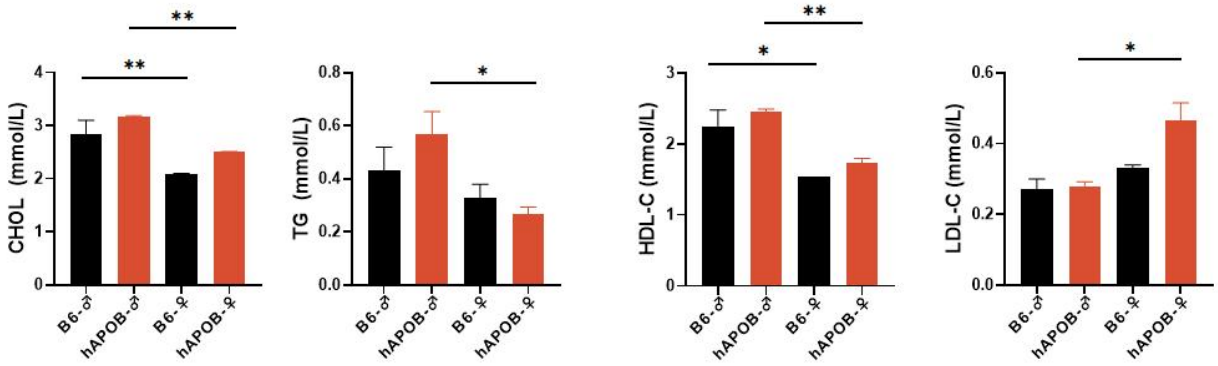

Fig 4. The blood lipid expression of B6-hAPOB-Tg(N2 generation) mice was similar to control mice
The blood lipid expression levels of B6 mice and hAPOB-N2 generation mice were detected by blood biochemical analyzer.The B6 group consisted of 7-8 weeks old B6 background mice (n=2; 2♂, 2♀); The hAPOB group consisted of 7-8 weeks old hAPOB-N2 generation mice（n=3; 3♂, 3♀).

References

1. Morita SY. Metabolism and Modification of Apolipoprotein B-Containing Lipoproteins Involved in Dyslipidemia and Atherosclerosis. Biol Pharm Bull. 2016;39(1):1-24.
2. Whitfield AJ, Barrett PH, van Bockxmeer FM, Burnett JR. Lipid disorders and mutations in the APOB gene. Clin Chem. 2004;50(10):1725-1732.
3. Voyiaziakis E, Ko C, O'Rourke SM, Huang LS. Genetic control of hepatic apoB-100 secretion in human apoB transgenic mouse strains. J Lipid Res. 1999;40(11):2004-2012.
4. Sirwi A, Hussain MM. Lipid transfer proteins in the assembly of apoB-containing lipoproteins. J Lipid Res. 2018;59(7):1094-1102.