B6-hDGAT2

Strain Name： B6/JGpt-Tg(hAPOE-DGAT2-LE1)/Gpt
Strain Type： Transgenic
Strain Number： T058211
Background： C57BL/6JGpt

Description

Non-alcoholic fatty liver disease (NAFLD) has a global prevalence of about 25%, is characterised by excessive accumulation of intrahepatic lipids, especially triglycerides (steatosis)[1]. A progressive subtype of the disease, non-alcoholic steatohepatitis (NASH), is characterized by cellular injury and inflammation[2], further deterioration can develop into cirrhosis and even liver cancer [3]. DGAT2 (Diacylglycerol acyltransferase 2) is mainly expressed in the liver and as a rate-limiting enzyme for *de novo* synthesis of triglycerides. Overexpression of DGAT2 may lead to increased accumulation of triglycerides in the liver and thus accelerate the progression of NAFLD. Although the exact molecular mechanism of NASH progression remains unclear, it has been reported that fat accumulation may be a major driving factor in the development of the disease, therefore DGAT2 is an important target for targeted therapy of NASH[4].

GemPharmatech used transgenic technology to produce a humanized DGAT2 mouse model carrying the human ApoE promoter, DGAT2 cDNA and LE1 element. This strain can successfully express human DGAT2, the humanized model of DGAT2 is an ideal animal model for drug development of metabolic diseases such as NAFLD and NASH.

Strategy

Fig.1 Schematic diagram of B6-hAPOE-DGAT2-LE1 model strategy

Applications

1. NAFLD and NASH research
2. The drug development of NAFLD and NASH: DGAT2 inhibititor, small interfering RNA (siRNA) targeting DGAT2

Data support

1. Detection of the level of hDGAT2 mRNA

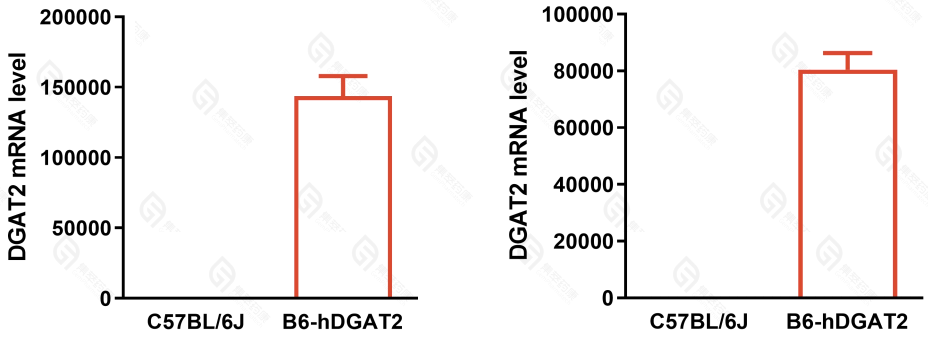

Fig 2. Detection of hDGAT2 expression in B6-hAPOE-DGAT2-LE1 mice

The human *DGAT2* is highly expressed in the liver tissues of B6-hAPOE-DGAT2-LE1 mice. On the left is generation F1 (B6, n=3, 1♂, 2♀; B6-hAPOE-DGAT2-LE1, n=4, ♀; on the right is the generation N2 (B6, n=6, 3♂ and 3♀; B6-hAPOE-DGAT2-LE1, n=6, 3♂ and 3♀).

2. Detection of the level of TG in plasma and liver

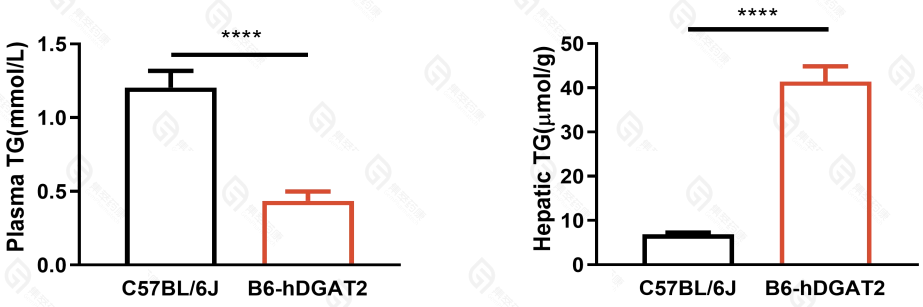

Fig 3. The level of TG in plasma and liver

The plasma TG of B6-hAPOE-DGAT2-LE1 mice is significantly decreased and the hepatic TG is significantly increased compared with C57BL/6J control. The level of TG in the plasma (left panel) and liver (right panel) of B6 and B6-hAPOE-DGAT2-LE1 mice (B6, n=6, ♀, 6 weeks; B6-hAPOE-DGAT2-LE1, n=7, ♀, 7-16 weeks).

References

1. Younossi ZM., et al. "Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes." Hepatology. 2016 Jul;64(1):73-84.

2. Review Team., et al. "World Gastroenterology Organisation global guidelines: Nonalcoholic fatty liver disease and nonalcoholic steatohepatitis." J Clin Gastroenterol. 2014 Jul;48(6):467-73.
3. Diehl AM., et al. "Cause, Pathogenesis, and Treatment of Nonalcoholic Steatohepatitis." N Engl J Med. 2017 Nov 23;377(21):2063-2072.
4. Yenilmez B., et al. "An RNAi therapeutic targeting hepatic DGAT2 in a genetically obese mouse model of nonalcoholic steatohepatitis." Mol Ther. 2022 Mar 2;30(3):1329-1342.