B6-Ldlr-KO

Strain Name: B6/JGpt-Ldlr^{em1Cd82}/Gpt
Strain Type: Cas9-KO
Strain ID: T001464
Background: C57BL/6JGpt

Description

LDLR（Low-Density Lipoprotein Receptor）known as LDL receptor，is a member of low density lipoprotein receptor family.LDL receptor can clear low-density lipoprotein (LDL) and intermediate-density lipoprotein (IDL) to regulate plasma cholesterol levels [1]。The researches have shown that Ldlr-deficient mice is twice the plasma total cholesterol levels that of wild-type, and low- density lipoprotein receptors are sensitive to hypercholesterolemia[2]. In addition, overexpression of the Ldlr gene in mice inhibits plasma hypercholesterolemia caused by a high cholesterol diet[3]. The Ldlr gene-deficient mouse model is significant for the clinical study of diabetic nephropathy, atherosclerosis, hyperlipemia and hyperglycemia.

Gempharmatech company knocked out the Ldlr gene of C57BL/6 mice using gene editing technology to establish an Ldlr knockout mouse model. The Ldlr knockout mice can not express LDLR protein and increase the blood lipid concentration significantly. The Ldlr knockout mice fed with high-fat diets causes atherosclerosis in early stage, which could be used for cardiovascular disease and Alzheimer's disease.

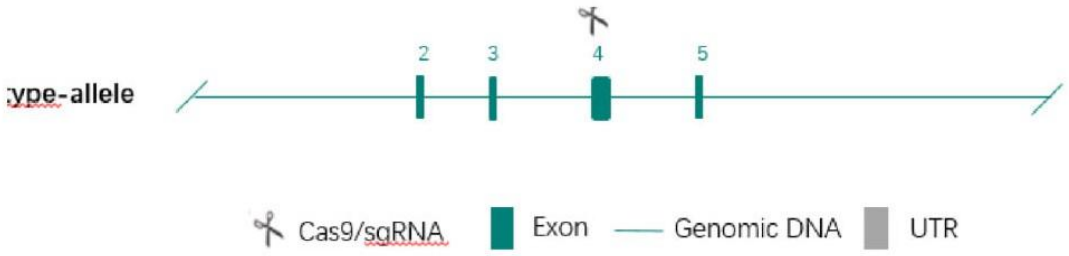

Fig1: Schematic diagram of Ldlr knockout strategy in Ldlr mice.

Applications

1. Pathophysiological study of atherosclerosis and cardiovascular disease
2. Screening of vasodilators
3. The development of AS diagnostic kit

Data support

1. Body weight

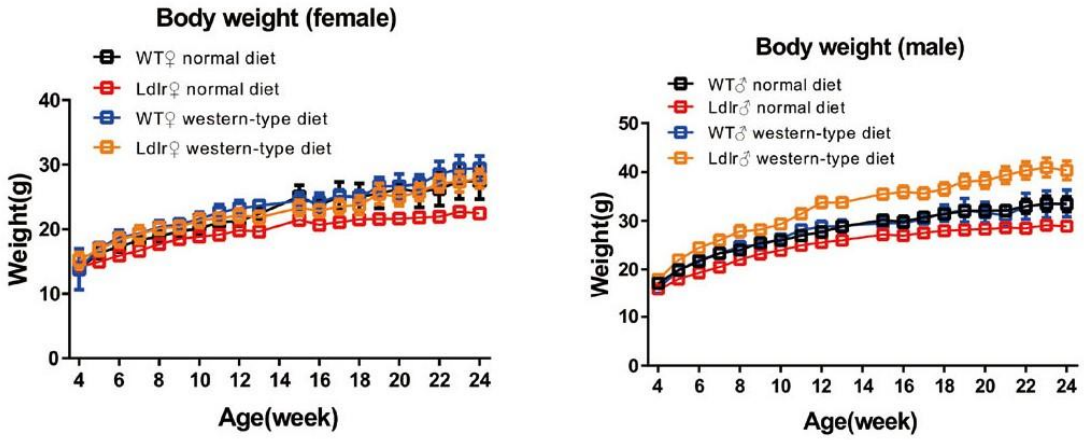

Fig 2. Body weight test of Ldlr-KO mice.

Mice were divided into groups with different feeds and body weights were measured from the 4th week, and measured every 2 weeks. The body weight changes of wild-type mice and Ldlr-ko mice under normal diet and high fat diet were tested. The results showed that the body weight trends of the two groups of mice were similar, and there was no significant difference.

2. Oil Red O staining of Aortic arch

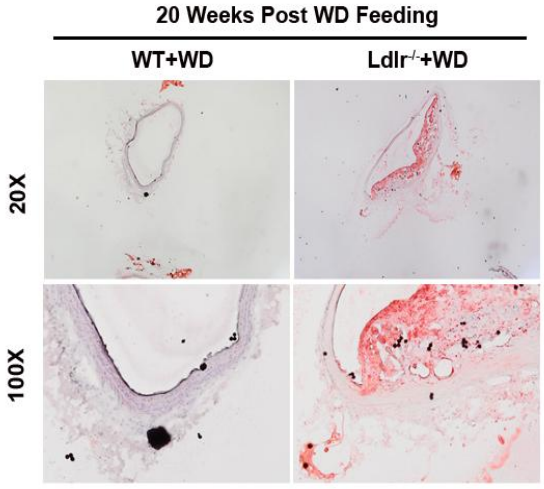

Fig 3. Observation of Aortic arch pathology with oil red O staining.

The aortic arch of wt and Ldlr mice fed with the high fat diet were isolated at 20 weeks, and pathological changes of the aortic wall were observed with oil red O staining.

The results showed that the inner wall of the aorta of Ldlr knockout mice causes local wall thickening with the lipid adhesion, which is the initial phenotype of atherosclerosis.
The results showed that 40% high fat diet would induce atherosclerosis of Ldlr knockout mice.

3. Blood lipid testing

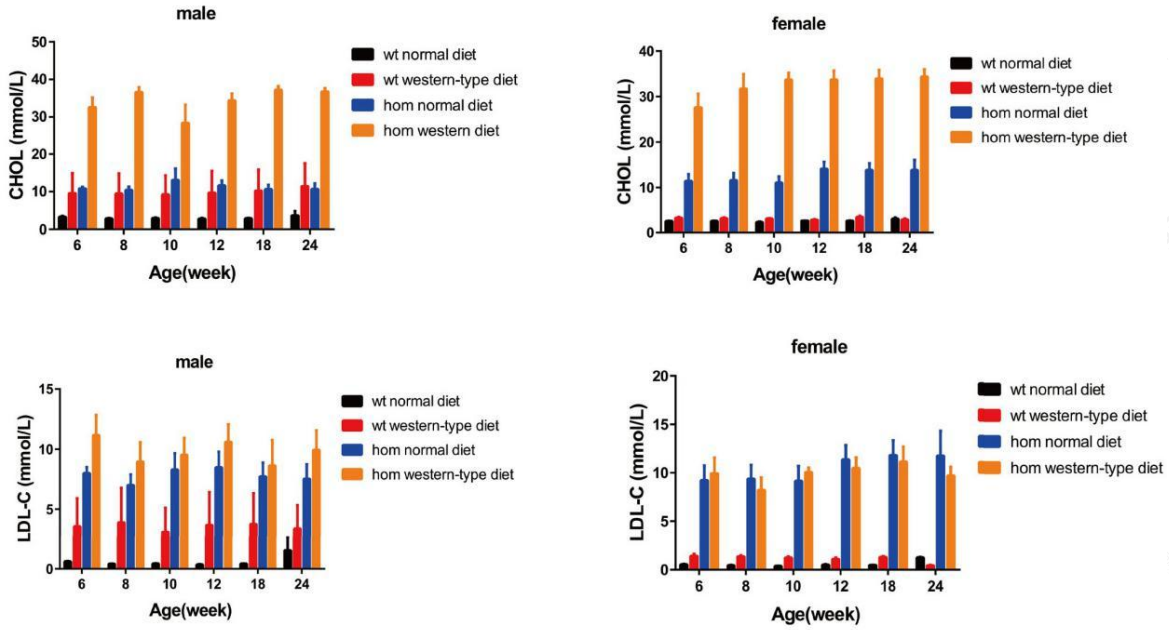

Fig 4. Blood lipid test of Ldlr mice.

Mice were divided into groups with different feeds and body weights were measured from the 4th week, a nd blood lipids were measured at 6, 8, 10, 12, 18, 24 weeks, respectively. Compared with wild male mice, CHOL content in the blood of Ldlr-/- mice is 2-3 times and LDL-c content is 3-5 times after 6 weeks of normal diet or high-fat diet. Compared with wild females, the levels of CHOL and LDL-c in the blood of Ldlr-/- mice is 5-10 times after 6 weeks on a normal diet or a high-fat diet. CHOL: cholesterol; LDL-c: Low Density Lipoprotein.

References

1. Brown, Michael S., and Joseph L. Goldstein. "A receptor-mediated pathway for cholesterol homeostasis." Science232.4746(1986): 34-47.
2. Ishibashi, Shun, et al. "Hypercholesterolemia in low density lipoprotein receptor knockout mice and its reversal by adenovirusmediated gene delivery." The Journal of clinical investigation 92.2 (1993): 883-893.
3. Yokode, Masayuki, et al. "Diet-induced hypercholesterolemia in mice: prevention by overexpression of LDL receptors." Science 250.4985 (1990): 1273-1275.Guy CT; Cardiff RD; Muller WJ. 1992. Induction of mammary tumors by expression of polyomavirus middle T oncogene: a transgenic mouse model for metastatic disease. Mol Cell Biol 12(3):954-61.