Apoe-KO

Strain Name: C57BL/6JGpt-*Apoe*^{em1Cd82}/Gpt
Strain Type: Knock-out
Strain ID: T001458
Background: C57BL/6JGpt

Description

APOE is primarily responsible for the transport of lipoproteins, fat-soluble vitamins and cholesterol. In peripheral tissues, APOE is mainly produced on liver and macrophages and mediates cholesterol metabolism. In the central nervous system, APOE is mainly produced by astrocytes, which transports cholesterol to neurons through APOE receptors. In addition, APOE is the main carrier of cholesterol in the brain [1].
The researches show that the defect of APOE mice is impaired in scavenging the chylomicron, VLDL and LDL of plasma and cholesterol content is significantly increased [2]. Apoe mice are extremely sensitive to cholesterol. When cholesterol enters the plasma, it accumulates. At about 3 months, fat streaks appears near the aorta and forming a pre-atherosclerotic lesion ages with age. Older *Apoe*-deficient mice (over 17 months) will have xanthoma lesion composed of crystalline cholesterol clots, lipid droplets, and foam cells, with smaller xanthoma seen in the choroid plexus and ventral tendon. The study also found that Apoe knockout mice have learning and memory diability [2].

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

Strategy

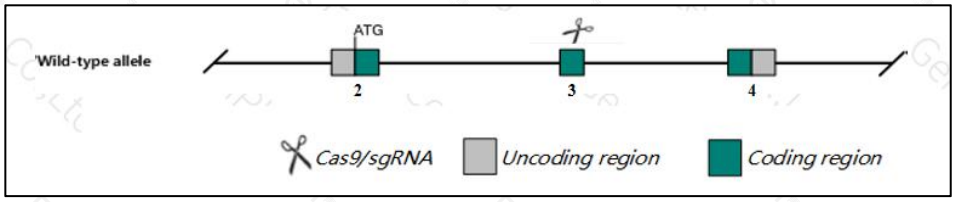

Fig1. Schematic diagram of Apoe-KO model strategy.

Applications

1. Cardiovascular Research: Atherosclerosis, Hypercholesterolemia, Hyperlipidemia
2. Lipid metabolism research
3. Neurobiology research: Alzheimer's disease, behavioral and learning disabilities disease, neurodegenerative diseases

Data support

1. Determination of APOE protein expression

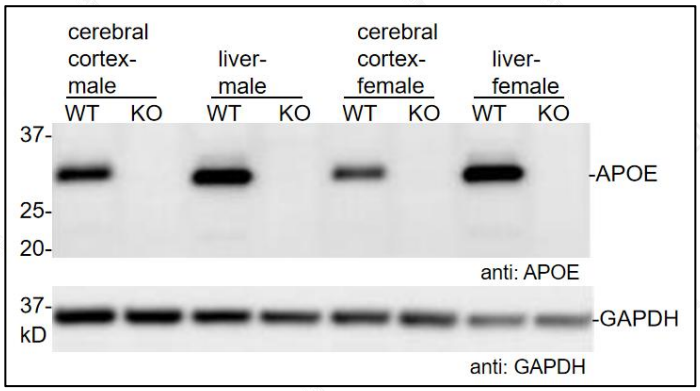

Fig2. Protein expression of APOE in cerebrum and liver tissues.

Protein expression of APOE in cerebrum and liver tissues was determined by Western Blot using specific antibody (Abcam, ab183596). WT: C57BL/6JGpt wildtype mice and KO: Apoe-KO homozygous mice. (Data source: Abcam collaborative verification).

2. IHC analysis of APOE

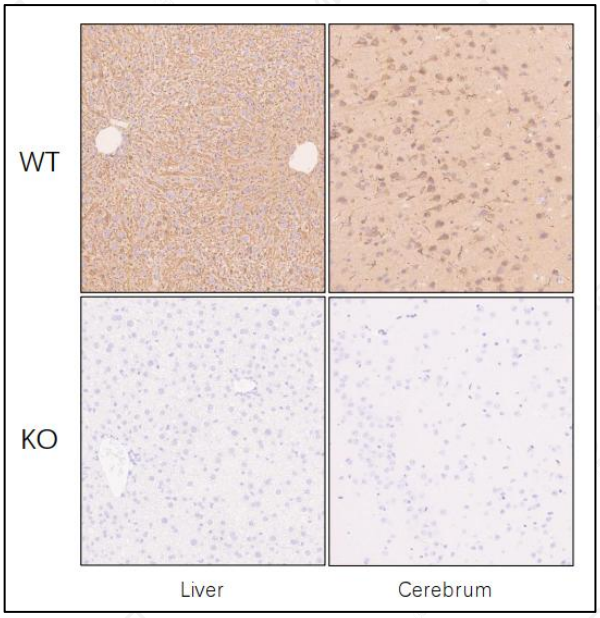

Fig3. Representative IHC of APOE in cerebrum and liver tissues.

IHC analysis of APOE in cerebrum and liver tissues using specific antibody (Abcam, ab183596). WT: C57BL/6JGpt wildtype mice and KO: Apoe-KO homozygous mice. (Data source: Abcam collaborative verification).

3. Detection of body weight

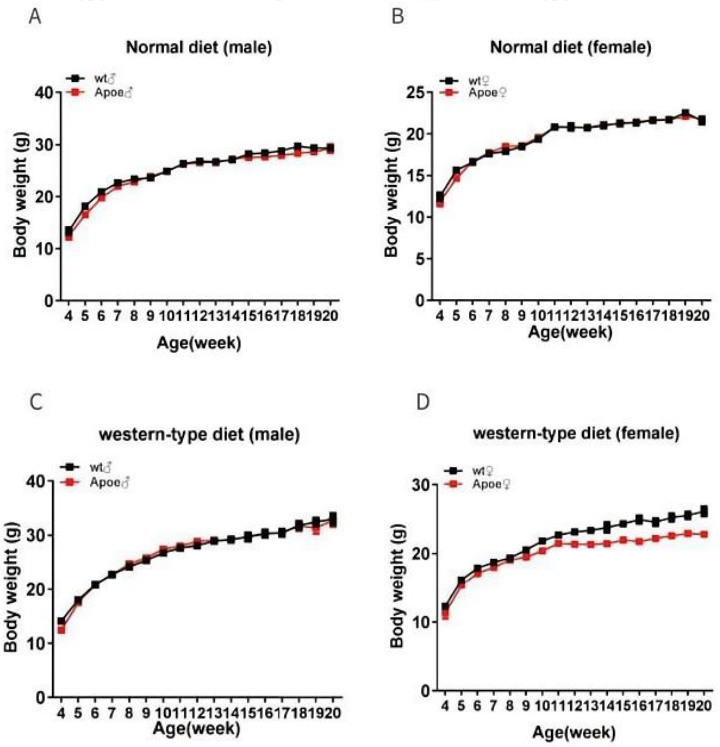

Fig4. Detection of body weight levels in Apoe$^{-/-}$ mice.

Wild-type mice and Apoe$^{-/-}$ mice were detectd for body weight levels under normal diet (A&B) and western diet (C&D). Apoe$^{-/-}$ mice group and wild-type mice group had a similar trend of body weight change, and there was no significant difference.

4. Detection of blood lipid

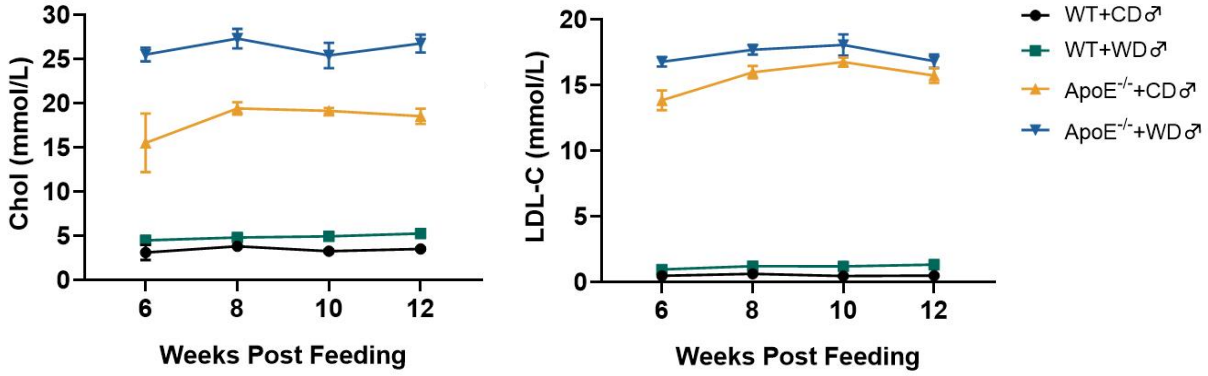

Fig5. Detection of blood lipids in Apoe$^{-/-}$ mice.

Compared with wild-type mice, Cholesterol and LDL-C levels were significantly increased in Western diet (WD) fed Apoe$^{-/-}$ mice.

5. Oil red O staining

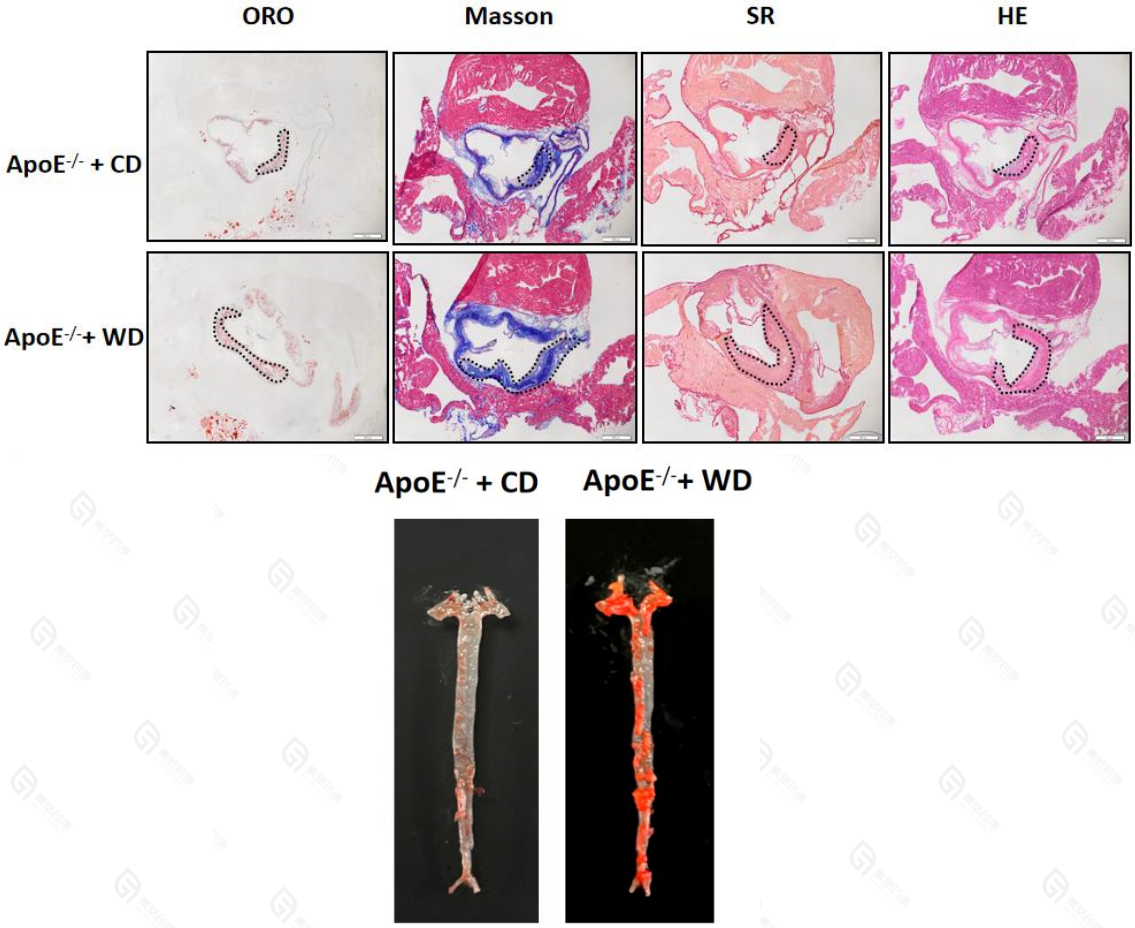

Fig6. Oil Red O staining of Apoe$^{-/-}$ mice aortic root.

ApoE$^{-/-}$ mice were fed with chow diet (CD) and western diet (WD) starting from 6 weeks of age. After 18 weeks, atherosclerotic plaques could be observed in the aortic root by Oil red O, Masson, Sirius Red and HE staining. Oil red O and HE staining can indicate the location of the plaque, while Masson and Sirius Red staining indicate the location of the fibrous cap on the plaque(marked by black dotted circle). Lipid-rich plaques (Red) also can be deteced by Oil red O staining of the whole aorta.

Biochemical Indicators

1. Blood routine

Parameter	Units	Males	Females
Hematology			
Age	weeks	16	16
WBC	K/uL	4.76	4.14
RBC	M/uL	10.17	9.78
Hb	g/L	146.26	141.17
HCT	%	42.13	40.83
MCV	fL	41.46	41.77

MCH	Pg	14.39	14.44
MCHC	g/L	347.17	345.83
RDW	%	18.61	18.19
PLT	K/uL	954.48	767.83
MPV	fL	4.2	4.16
NE#	K/uL	0.71	0.78
NE%	%	14.57	19.01
LY#	K/uL	3.88	3.18
LY%	%	81.74	76.76
EO#	K/uL	0.01	0.01
EO%	%	0.17	0.15
MO#	K/uL	0.17	0.17
MO%	%	3.46	4.02
BA#	K/uL	0	0
BA%	%	0.06	0.06

2. Blood Biochemistry

Parameter	Units	Males	Females
Biochemistry			
Age	weeks	16	16
ALT	IU/L	32.48	25
AST	IU/L	72.9	71.21
TP	g/dL	6.11	5.32
ALB	g/dL	3.8	3.7
AKP	IU/L	143.14	237.75
TBIL	umol/L	1.63	1.93
BUN	mmol/L	9.09	8.8
CREA	umol/L	13.9	12.75
CHOl	mmol/L	17.69	16.03
TG	mmol/L	1.27	0.54
HDL-C	mmol/L	2.46	2.2
LDL-C	mmol/L	16.49	14.74
Ca	mmol/L	2.63	2.47
P	mmol/L	3.85	3.23
Fe	umol/L	17.29	17.51
GLU	mmol/L	6.2	5.59

Related Products

T001464 Ldlr-KO

Precautions

1. mice feed

Apoe-KO mice need to pay attention to the quality of their daily feeding. The type and content of fat in the model feed and the level of cholesterol are critical for animal function and the reliability and reproducibility of research results.

2. The difference between Apoe-KO and Ldlr-KO model of atherosclerosis

Apoe-KO is a spontaneous atherosclerosis model, which is more similar to the human atherosclerosis process. The plasma total cholesterol level of Apoe-KO mice was higher than that of normal mice, and the total cholesterol level did not change with gender and age. At 3 months of age, fatty streaks can be found near the aorta, and the lesions increase with age. During the course of the disease, there is less lipid but more slender cells, which is typical of the early stage of atherosclerotic lesions. At 13 months of age, the atherosclerotic lesions in the mice extended from the carotid artery, heart and aorta to the renal artery and iliac bifurcation.

Ldlr-KO developed atherosclerotic plaques only when fed a high cholesterol diet, and normal diets could not induce the appearance of plaques. After 16 weeks of high-cholesterol diet: mice developed extensive aortic intimal thickening and 60%-80% of the surface Sudan staining positive, endothelial rupture in atherosclerotic lesions, and accumulation of macrophages and foam cells.

Publications

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2. S Xu, H Ni, H Chen, Q Dai. et al. The interaction between STAT3 and nAChRα1 interferes with nicotine-induced atherosclerosis via Akt/mTOR signaling cascade. Aging (Albany NY) . 2019 Oct 14; 11(19): 8120-8138. DOI: 10. 18632/aging. 102296. 【APOE. T001458】
3. G Miao, X Zhao, B Wang, L Zhang. et al. TLR2/CXCR4 coassociation facilitates Chlamydia pneumoniae infection-induced atherosclerosis. Heart and circulatory physiology. 2020, Jun 1; 318(6): H1420-H1435. DOI: 10. 1152/ajpheart. 00011. 2020. 【APOE. T001458. Tlr2-KO.T006733】
4. H Ni, S Xu, H Chen, Q Dai. et al. Nicotine modulates CTSS (Cathepsin S) synthesis and secretion through regulating the autophagy-lysosomal machinery in atherosclerosis. Arteriosclerosis, Thrombosis, and Vascular Biology. 2020, Sep; 40(9): 2054-2069. DOI: 10. 1161/ATVBAHA. 120. 314053. 【APOE. T001458】

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8. S Xu, H Chen, H Ni, Q Dai. et al. Targeting HDAC6 attenuates nicotine-induced macrophage pyroptosis via NF-κB/NLRP3 pathway. Atherosclerosis. 2021 ; 317:1-9. DOI: 10. 1016/j. atherosclerosis. 2020. 11. 021. 【APOE. T001458】
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10. Zeng P, Yang J, Liu L, et al. ERK1/2 inhibition reduces vascular calcification by activating miR-126-3p-DKK1/LRP6 pathway. Theranostics. 2021 Jan 1; 11(3): 1129-1146. DOI: 10.7150/thno.49771.【ApoE deficient (apoE-/-). T001458】

References

1. Piedrahita, Jorge A., et al. "Generation of mice carrying a mutant apolipoprotein E gene inactivated by gene targeting in embryonic stem cells." Proceedings of the National Academy of Sciences 89.10 (1992): 4471-4475.
2. MOGHADASIAN, MOHAMMED H., et al. "Pathophysiology of apolipoprotein E deficiency in mice: relevance to apo E-related disorders in humans." The FASEB Journal 15.14 (2001): 2623-2630.