

C001368

Strain Datasheet



Lep KO (ob/ob) Mouse

Product ID: C001368

Common Name: Lep KO (ob/ob)

Strain Name: C57BL/6JCya-Lep^{em1(R105X)}/Cya

Background: C57BL/6JCya

🔗 Strain Description

The leptin (LEP) gene, also known as the OB gene, encodes the leptin protein, which is secreted into the circulation by white adipocytes and plays a major role in the regulation of energy homeostasis.

Circulating leptin binds to leptin receptors (LEPR) in the brain, activating downstream signaling pathways that inhibit feeding and promote energy expenditure. Leptin also has multiple endocrine functions and is involved in physiopathological processes such as immune and inflammatory responses, hematopoiesis, angiogenesis, reproduction, bone formation, and wound healing ^[1]. Mutations in the LEP gene and its regulatory regions lead to severe obesity and morbid obesity with hypogonadism in humans and are also associated with the development of type II diabetes ^[2].

This strain is a Lep deletion mouse model that uses gene editing technology to knock out the expression of human LEP gene homolog in mice with impaired leptin synthesis. According to the literature, this mouse model exhibits obesity, excessive food intake, transient hyperglycemia, poor glucose tolerance, and elevated plasma insulin, accompanied by hypometabolism, hypothermia, and low fertility, in addition to impaired wound healing and increased production of hormones by their pituitary and

adrenal glands ^[3]; The phenotype is more similar to that of type II diabetes and obesity in stages I and II, with an increase in the number and size are increased, which can be used in obesity and type II diabetes studies. Homozygous Lep KO mice are viable but the females are sterile and the males have reduced fecundity.

Application Area

- ① The Lep KO mice can be used for the study of type II diabetes, obesity diseases, endocrine defects, and other metabolic diseases.

Strain Strategy

A 2-base deletion mutation was introduced in Exon3 of the Lep gene in C57BL/6JCya mice to obtain the Lep KO mouse model.



Figure 1. Diagram of the gene editing strategy for the generation of Lep KO mice.

Validation Data

1. Growth Curve

Compared with the wild-type control group (WT), the weight of male Lep KO mice (ob/ob) increased rapidly from 5 to 12 weeks, slowly increased after 13 weeks, and was twice that of wild-type mice at 20 weeks. The weight change trend of female Lep KO mice is consistent with that of male mice.

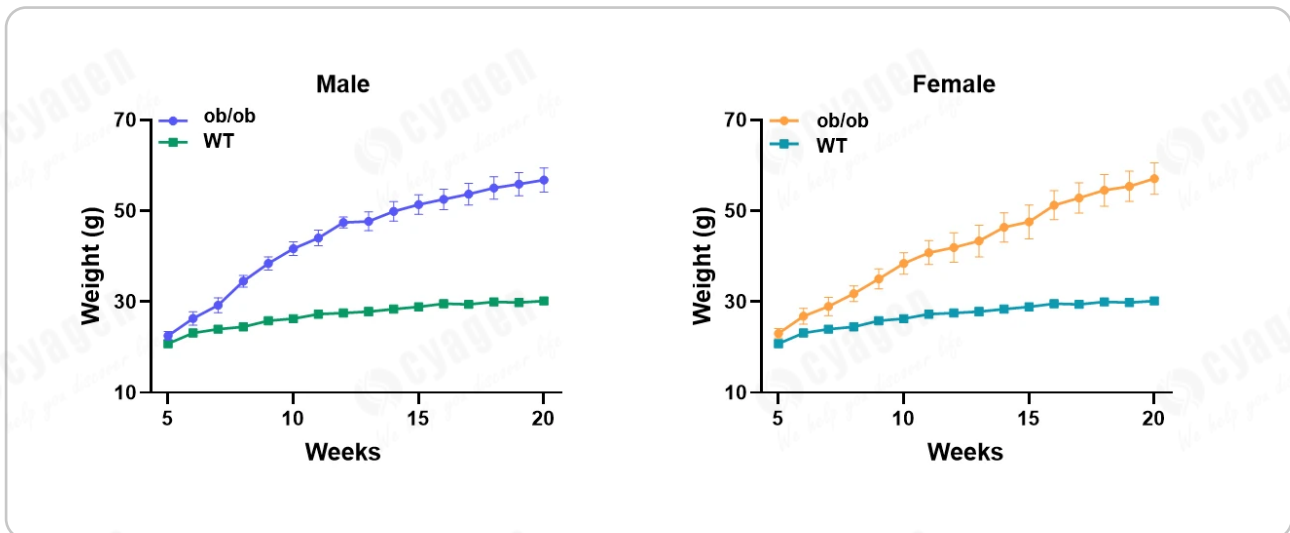


Figure 2. Growth curve of male and female Lep KO mice with wild-type mice.

2. Body Size Comparison

Both female (♂) and male (♀) Lep KO mice (right) showed a distinct obese phenotype compared to wild-type mice (left).



Figure 3. Body size of Lep KO mice compared with wild-type mice.

3. Random Blood Glucose

Compared with the wild-type control group (WT), the random blood glucose of male Lep KO mice (ob/ob) began to rise in week 7, began to decline after 13 weeks, and was similar to that of wild-type mice after 15 weeks. The random blood glucose of female Lep KO mice began to rise in week 6, began to decline after 14 weeks, and was slightly higher than that of wild-type mice.

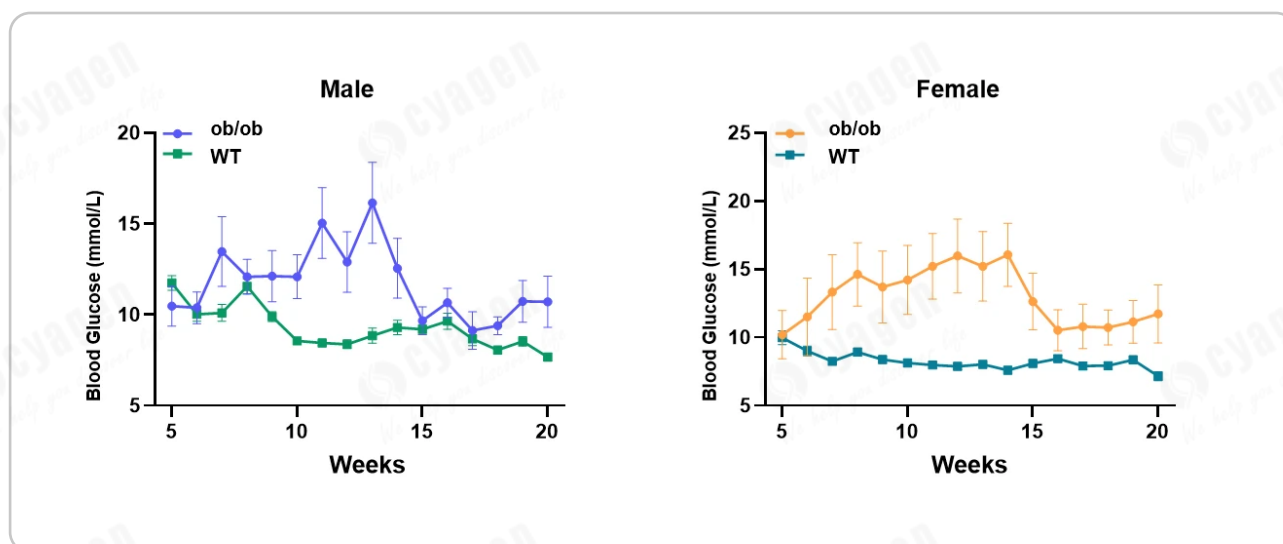


Figure 4. Random blood glucose levels between male and female Lep KO mice and wild-type mice.

4. Fasting Blood Glucose

Compared with the wild-type control group (WT), the fasting blood glucose of male Lep KO mice (ob/ob) began to decline after 12 weeks, fluctuated briefly, and was similar to that of wild-type mice. The fasting blood glucose of female Lep KO mice began to decline after 14 weeks, fluctuated briefly, and was similar to that of wild-type mice.

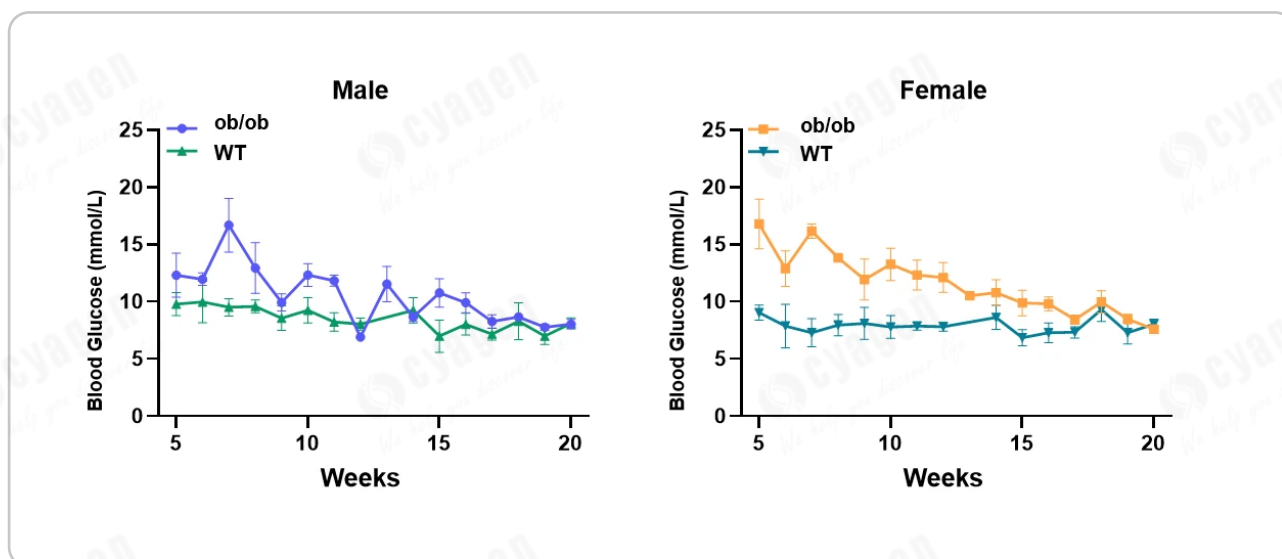


Figure 5. Fasting blood glucose levels between male and female Lep KO mice and wild-type mice.

5. Lipid Metabolism Parameters

Compared with the wild-type control group (WT), the various lipid metabolism parameters of male and female Lep KO mice were significantly increased, indicating that the mouse has an obvious hyperlipidemia phenotype.

***HDL-C:** high-density lipoprotein cholesterol; **LDL-C:** low-density lipoprotein cholesterol; **TC:** total cholesterol; **TG:** triglycerides.

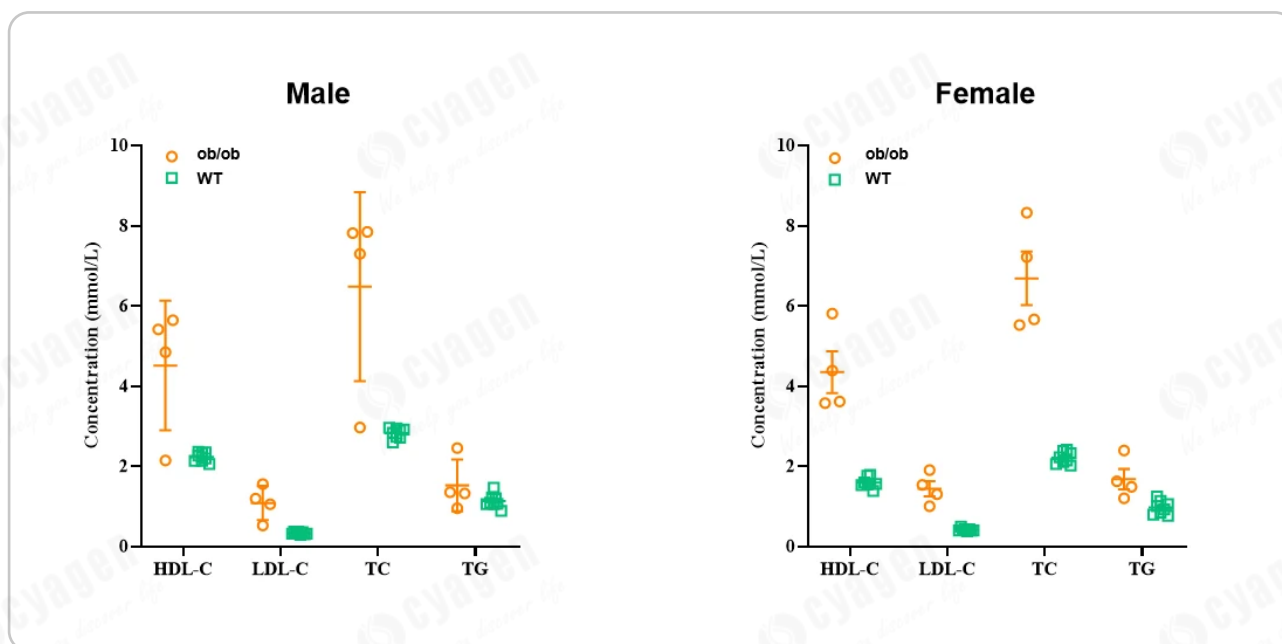


Figure 6. Lipid metabolism parameters between male and female Lep KO mice and wild-type mice.

6. Liver Function Tests

Compared with the wild-type control group (C57BL/6J WT), the various liver function indicators of male and female Lep KO mice were significantly increased, indicating that the mouse has obvious liver metabolic abnormalities.

***ALP:** alkaline phosphatase; **ALT:** alanine transaminase; **AST:** aspartate aminotransferase; **LDH:** lactate dehydrogenase.

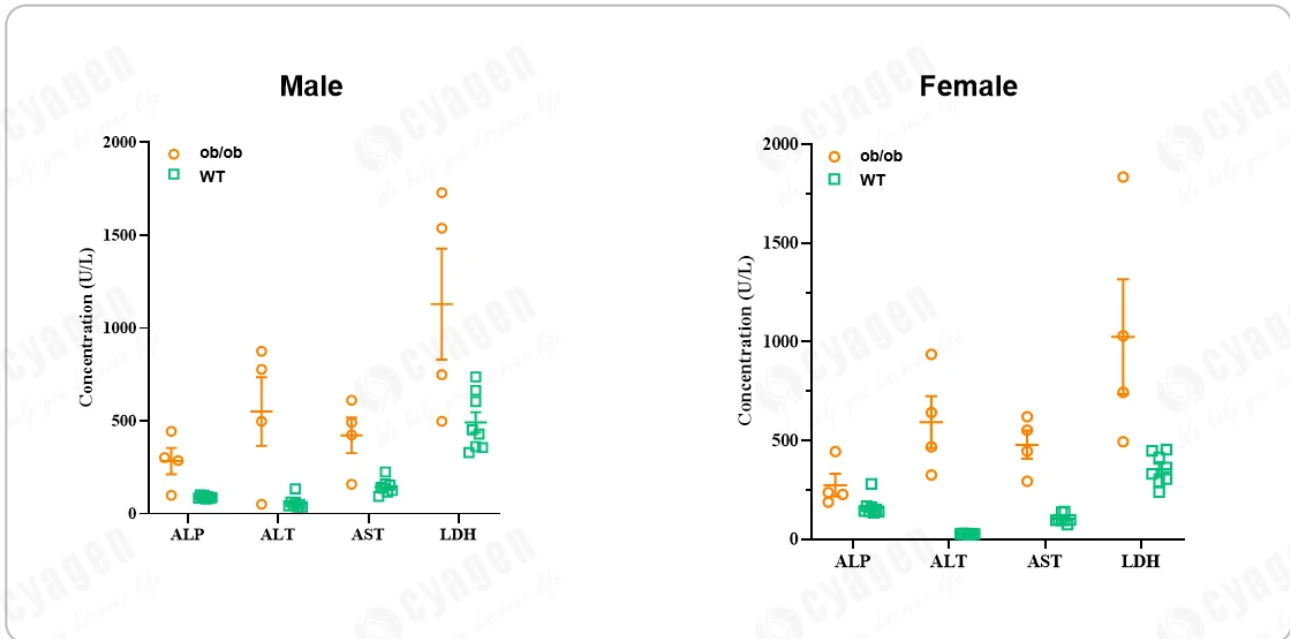


Figure 7. Liver function indicators between male and female Lep KO mice and wild-type mice.

Publications

Nature Communications 2023.11

SLC35D3 promotes white adipose tissue browning to ameliorate obesity by NOTCH signaling

Nature Communications 2024.04

AZGP1 in POMC neurons modulates energy homeostasis and metabolism through leptin-mediated STAT3 phosphorylation

Reference

[1]. Ahima RS, Flier JS. Leptin. Annu Rev Physiol. 2000;62:413-37.

- [2]. Livshits G, Pantsulaia I, Gerber LM. Association of leptin levels with obesity and blood pressure: possible common genetic variation. *Int J Obes (Lond)*. 2005 Jan;29(1):85–92. doi: 10.1038/sj.ijo.0802826. Erratum in: *Int J Obes Relat Metab Disord*. 2005 Apr;29(4):447.
- [3]. Trayhurn P. The development of obesity in animals: the role of genetic susceptibility. *Clin Endocrinol Metab*. 1984 Nov;13(3):451–74.

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