B6-Chr1^{YP1}

Strain Name: B6/JGpt-Chr1^{YP1}/Gpt

Strain Type: Wild mice (Chromosome Segment Substitution Lines)

Strain Number: D000750

Background: C57BL/6JGpt

Description

Metabolic syndrome (MetS) is a cluster of clinical manifestations including: (1) obesity, abdominal adiposity or insulin resistance, (2) impaired glucose metabolism, (3) hypertension, and (4) atherogenic dyslipidemia. Genetic factors are of great significance in MetS, which contributes to individual and interpersonal differences. The inbred genetic background of existing mouse models limits the in-depth research towards MetS, given the shared genetic background of each strain[1-3].

Gempharmatech generated wild mouse derived Chr1 substitution strains to enrich the genetic background and circumvent this limitation. Using wild mouse caught from different parts of China as donors, we established 11 wild-derived chromosome 1 substitution strains in the background of C57BL/6JGpt(B6J)[4]. Introducing chromosome 1 of wild mice into inbred mice with clear genetic background is beneficial to cloning and analysis of genes related to complex traits, and provides new resources for the analysis of new signaling pathways and disease mechanisms.

Through phenotype screening, we identified that **B6-Chr1YP1 mice** (**D000750, abbreviated as 750**) displayed obvious spontaneous MetS phenotypes, including accelerated increase in body weight and fat content as animals age, and the presence of early hepatic steatosis, glucose intolerance and insulin resistance which are absent among B6 mice.

Strategy

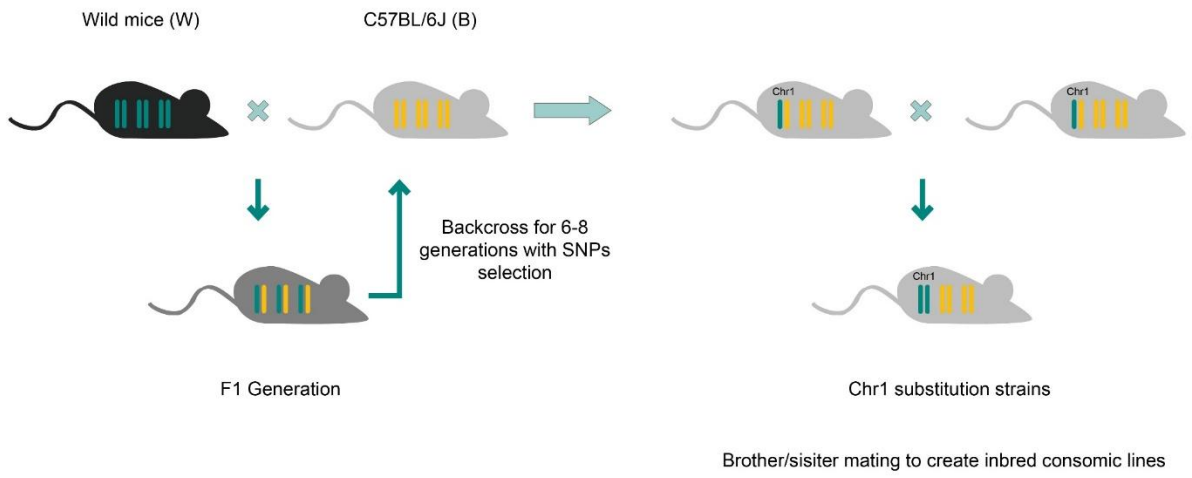

Fig.1 Schematic diagram of B6-Chr1^{YP1} strategy.

Applications

1. Screening and evaluation of therapeutic drugs for obesity, hyperlipidemia and fatty liver
2. Research on the mechanism of obesity, hyperlipidemia and fatty liver
3. Related studies on glucose metabolism and lipid metabolism

Data support

1. Body weight and fat ratio

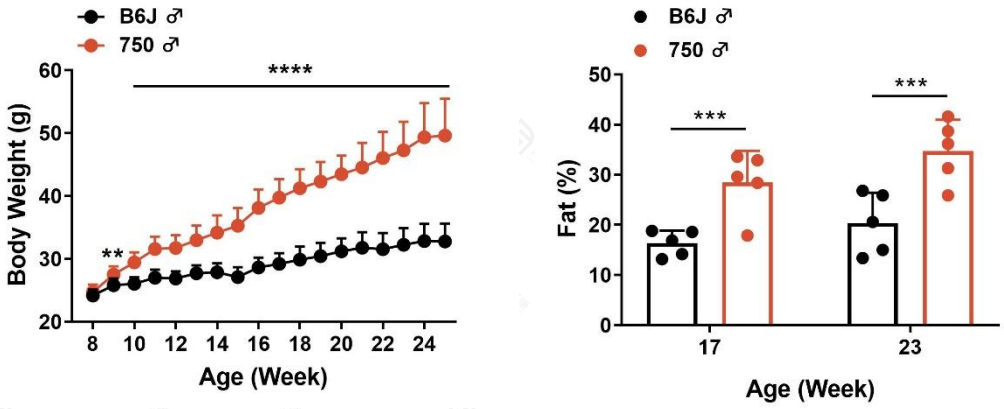

Fig 2. 750 mice showed spontaneous obesity phenotypes

There was no significant difference in body weight between male 750 and B6J before 10 weeks of age, and 750 mice displayed accelerated increase in body weight and fat content after 10 weeks of age. At 17

weeks of age and 23 weeks of age, the body fat ratio of 750 mice was significantly higher than that of control B6J males. N=8-10/group, and all data represent as MEAN ± SD.

2. Weight of adipose tissues and liver

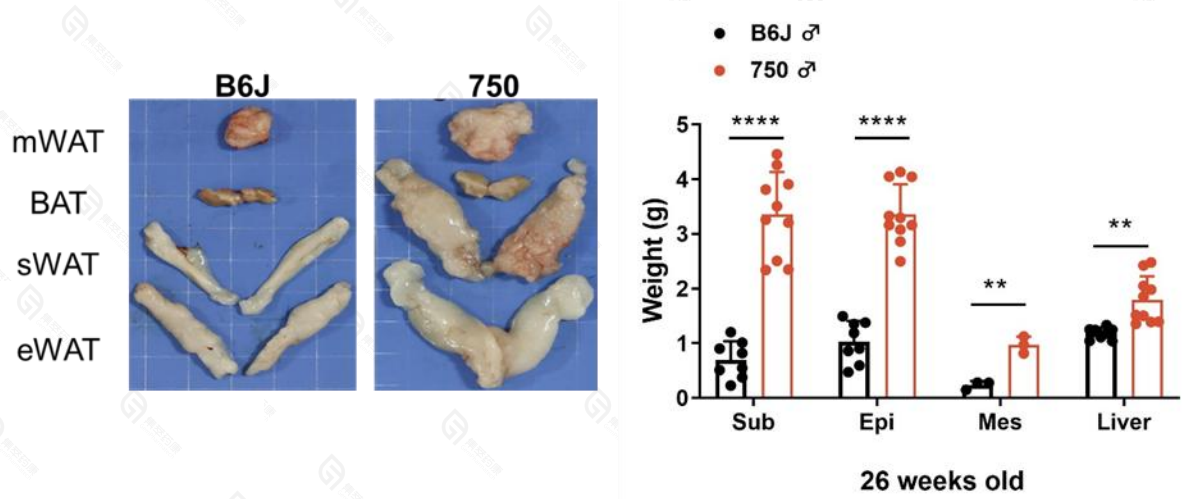

Fig 3. 750 mice had increased weight of adipose tissues and liver

The weight and the representative images of subcutaneous fat (sWAT), epididymis fat (eWAT), mesentery fat (mWAT), brown fat (BAT) and liver at the age of 26 weeks. N=8-10/group, and all data represent as MEAN ± SD.

3. Lipid profile on chow diet and western diet

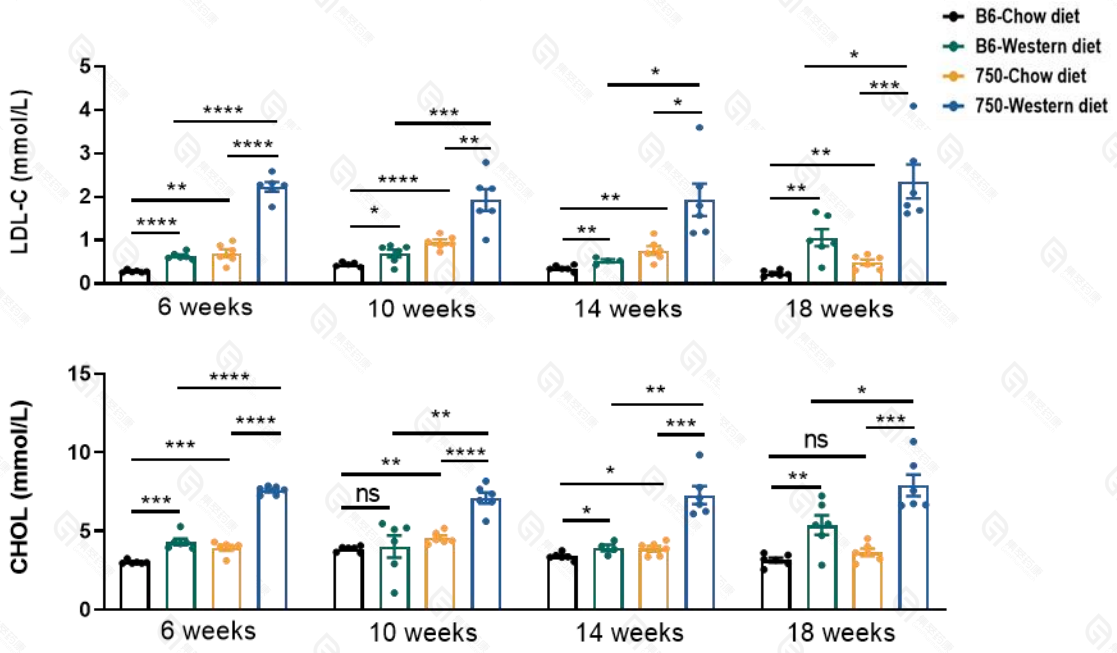

Fig 4. 750 mice displayed higher cholesterol than B6J mice

750 mice and B6J mice of 8 weeks of age were fed the chow diet and western diet for weeks. Plasma lipids were measured at 6, 10, 14 and 18 weeks post feeding. N=5-7/group, and all data represent as MEAN ± SD.

4. Liver pathology on chow diet and western diet

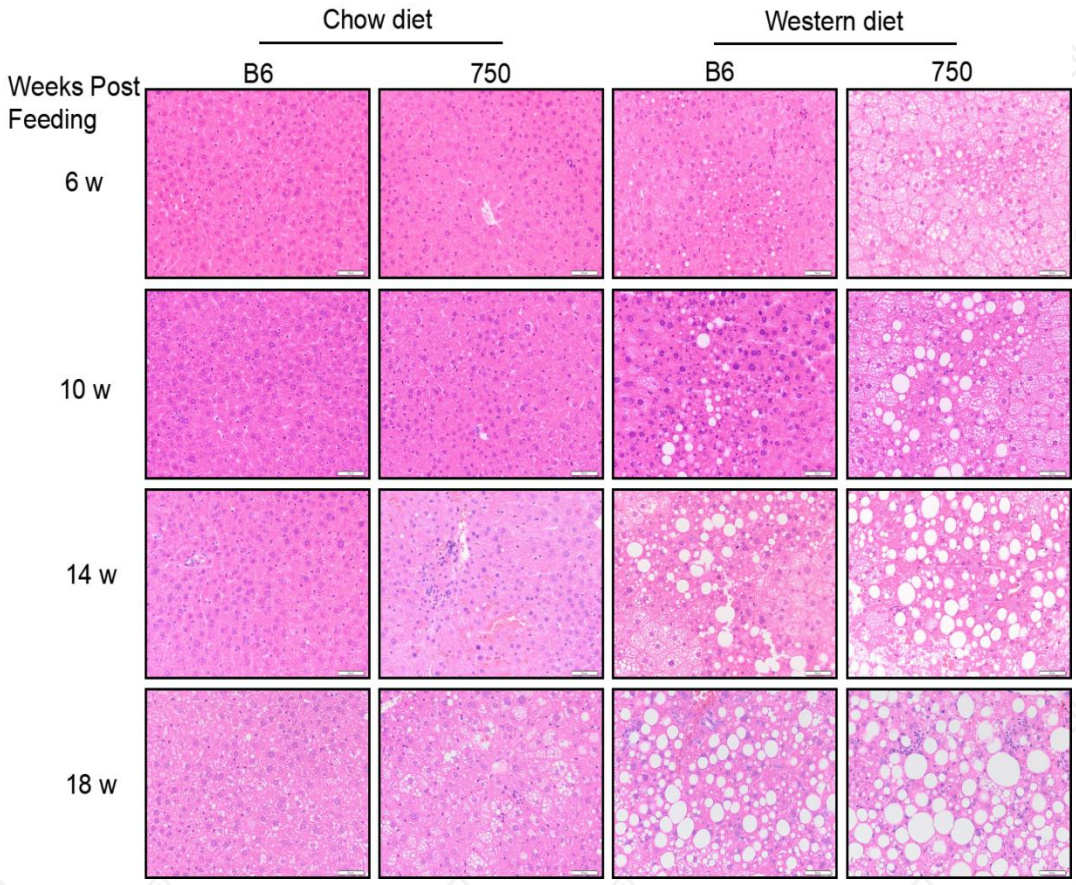

Fig 5. 750 mice displayed more severe NASH phenotype than B6J mice

750 mice and B6J mice at 8 weeks of age were fed with chow diet and western diet for weeks. Liver pathology was checked via H&E staining at 6, 10, 14 and 18 weeks post feeding. N=5-7/group, and the representative images were presented as above.

Precautions for use

1. The metabolic abnormalities of male 750 mice are more obvious, and no obvious abnormalities are observed in female 750 mice under chow diet. Body weight varies from different individuals, so it is recommended to leave about 10% surplus when ordering.
2. 750 mice are sensitive to dietary fat content, and diets with different fat content have significant effects on the weight gain of mice. It is recommended to select 6% fat diet as chow diet.

3. The body size of 750 mice is significantly bigger than that of B6J, so the feeding density should be reduced accordingly.

References

1. Aamir Zuberi and Cathleen Lutz. Mouse Models for Drug Discovery. Can New Tools and Technology Improve Translational Power. ILAR Journal, 2016, Vol. 57, No. 2, 178-185.
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3. Jean Louis Guénet, François Bonhomme. Wild mice: an ever-increasing contribution to a popular mammalian model. Trends Genet. 2003 Jan;19(1):24-31.
4. Xu Li, Minli Sun, Hao Qi et al. Identification of a Chromosome 1 Substitution Line B6-Chr1BLD as a Novel Hyperlipidemia Model via Phenotyping Screening. Metabolites.2022. 12, 1276.