Uox-KO

Strain Name： B6/JGpt-Uox^{em3Cd3501}/Gpt
Strain Type： Knock-out
Strain Number： T011801
Background： C57BL/6JGpt

Description

Urate oxidase UOX (Urate oxidase) is a class of uric acid catalyzing enzymes that can catalyze the oxidation of uric acid to allantoin. Uox genes are widely present in bacteria and mammals, but in humans and some primates, they become pseudogenes due to mutation and do not express UOX, resulting in uric acid as the end product of purine oxidation in humans and apes.

Hyperuricemia (HUA) is a metabolic disease caused by increased uric acid synthesis and/or decreased excretion. It is defined as fasting blood uric acid levels higher than 420 μmol/L on two different days under a normal purine diet. Hyperuricemia is a chronic, systemic disease that can lead to damage to multiple target organs, impair the prognosis and life quality of patients.

We knocked out exons 2-4 of the mouse Uox gene on the C57BL/6J background to obtain the Uox-KO model. This model is an ideal animal model for screening and evaluating drugs for treating hyperuricemia due to the accumulation of uric acid in mice due to the lack of UOX expression.

Strategy

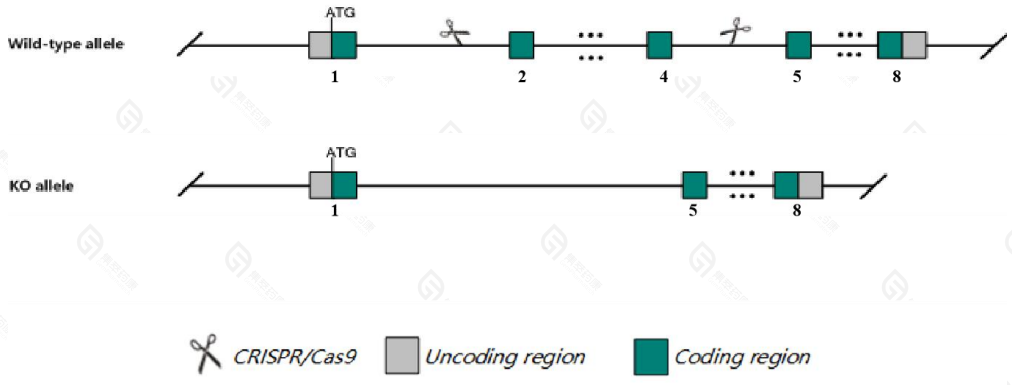

Fig.1 Schematic diagram of Uox-KO model stratery.

Applications

Spontaneous hyperuricemia disease model, to evaluate drugs for the treatment of hyperuricemia

Data support

1. mRNA expression of Uox gene

In Uox-KO mice, Uox gene expression could not be detected. In Uox heterozygous mice, the expression of Uox gene was decreased compared with the control group.

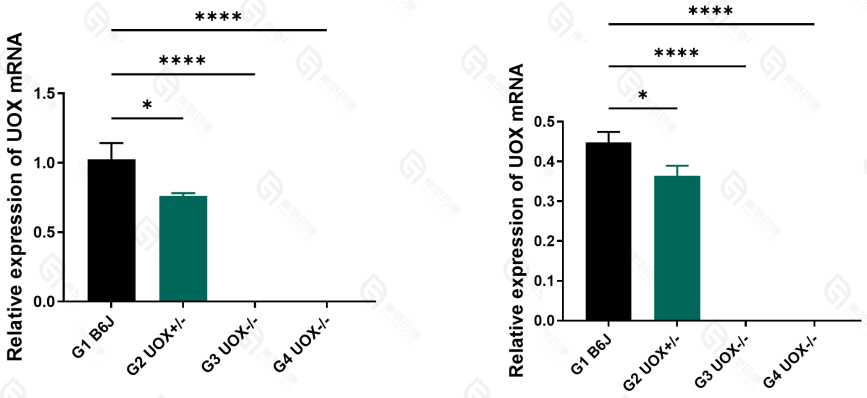

Fig 1. Detection of *Uox* expression in Uox-KO mice.

Note: n=5. Data are presented as Mean ± SEM and statistical analysis was performed using one-way ANOVA with Dunnett post-hoc test. *, P<0.05; **, P<0.01; ***, P<0.001; ****, P<0.0001

2. Uox protein expression

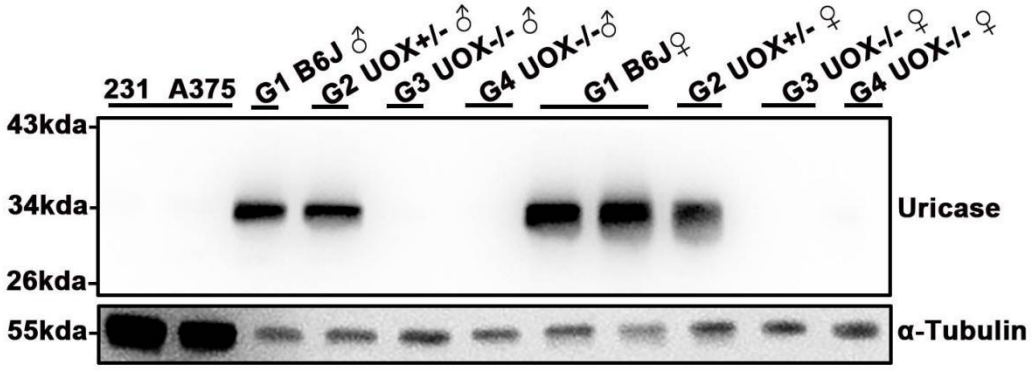

Fig 2. Protein expression of Uox in Uox-KO mice

In Uox-KO mice, Uox protein expression could not be detected. In Uox heterozygous mice, the expression of Uox protein was lower than that in the control group.

3. Efficacy validation

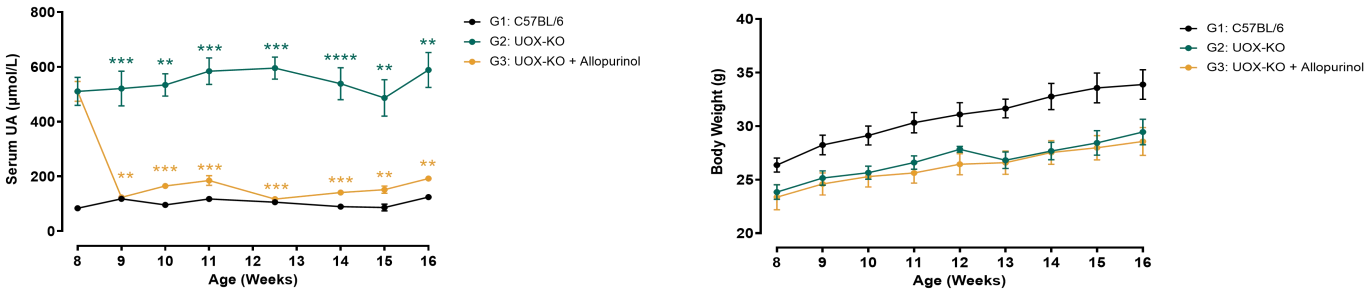

Figure 3. The serum uric acid levels and body weight changes in male mice

Note: n=5. Data are presented as Mean ± SEM and statistical analysis was performed using one-way ANOVA with Dunnett post-hoc test. *, P<0.05; **, P<0.01; ***, P<0.001; ****, P<0.0001.

The mice were divided into three groups: G1 - Healthy control group (C57BL/6), G2 - UOX knockout group (UOX-KO), and G3 - UOX-KO + Allopurinol intervention group (UOX-KO + Allopurinol). Compared to the male C57BL/6 mice in the G1 group, male UOX-KO mice in the G2 group exhibited a significant increase in serum uric acid levels, with serum uric acid values ranging from 400 to 600 umol/L at 8-16 weeks of age. In the G3 group, male UOX-KO mice showed a significant reduction in serum uric acid levels following allopurinol intervention (200μg/ml). These results indicate that male UOX-KO mice exhibit a significant elevation in serum uric acid levels, making them suitable models for hyperuricemia. Allopurinol intervention can significantly decrease the serum uric acid levels in male UOX-KO mice, with no impact on body weight.

References

1.Jie Lu, Xu Hou, Xuan Yuan, Lingling Cui, Zhen Liu, Xinde Li, Lidan Ma, Xiaoyu Cheng, et al." Knockout of the urate oxidase gene provides a stable mouse model of hyperuricemia associated with metabolic disorders." Kidney International 2018 Jan;93(1):69-80..