- Sichuan Provincial Medical Center, China
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Improved type 2 diabetes in ZDF rats through RYGB-mediated upregulation of hepatic TFF3 activating the Pl3K-AKT pathway

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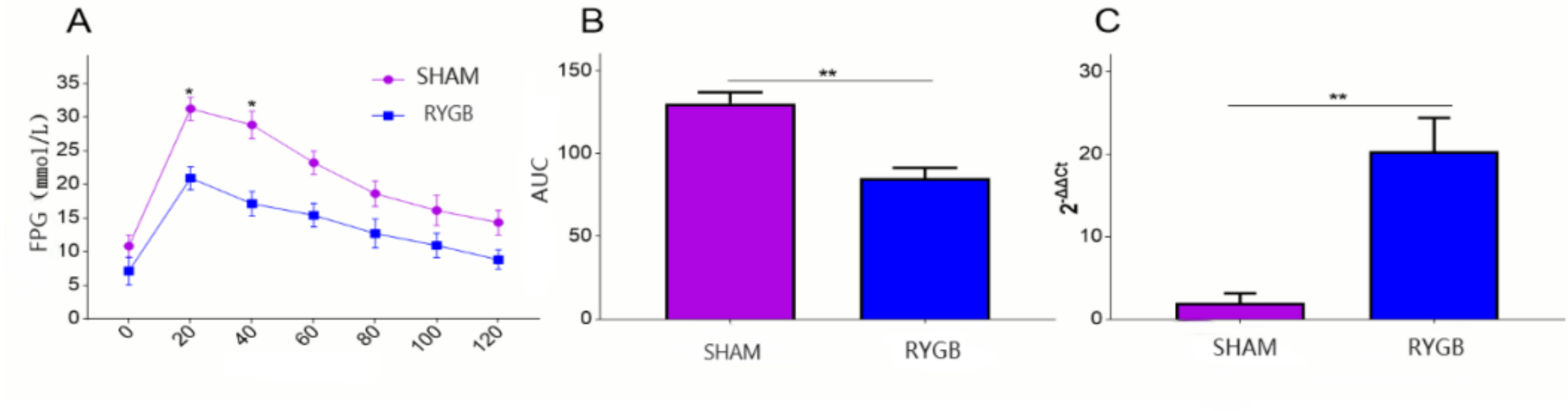
Research background

The latest data from the World Health Organization (WHO) shows that there are approximately 102.9 million people with diabetes in China, accounting for 24.4% of the global total and ranking first in the world. According to a report by the International Diabetes Federation, the number of people with type 2 diabetes worldwide is expected to increase to approximately 744 million by 2045.

Preliminary study

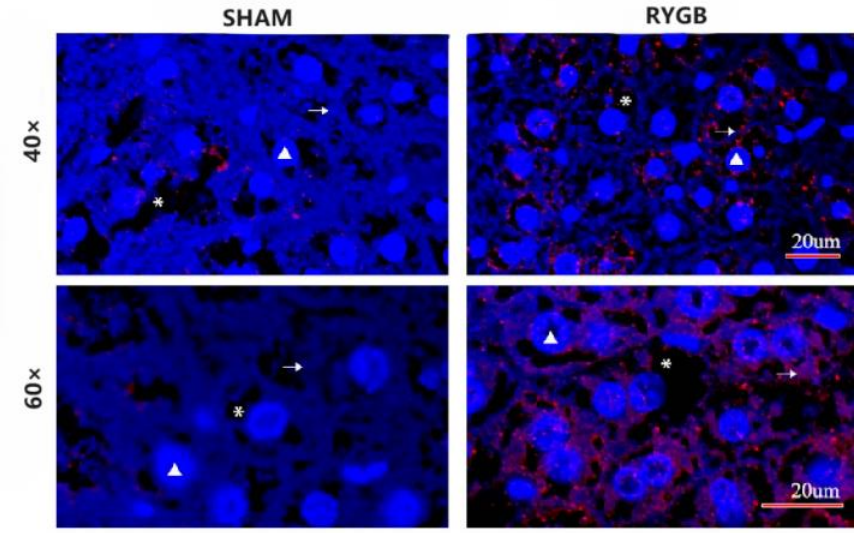


RYGB significantly improved blood glucose metabolism in Zucker diabetic-fatty (ZDF) rats (Figure A、B)

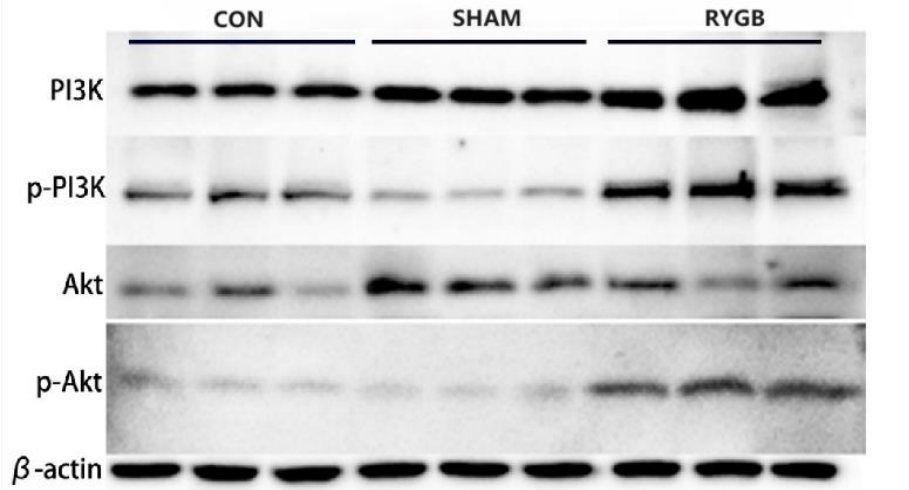
RYGB significantly up-regulated liver TFF3 expression (Figure C)

Preliminary study

RYGB significantly upregulated liver TFF3 expression (Immunofluorescence)

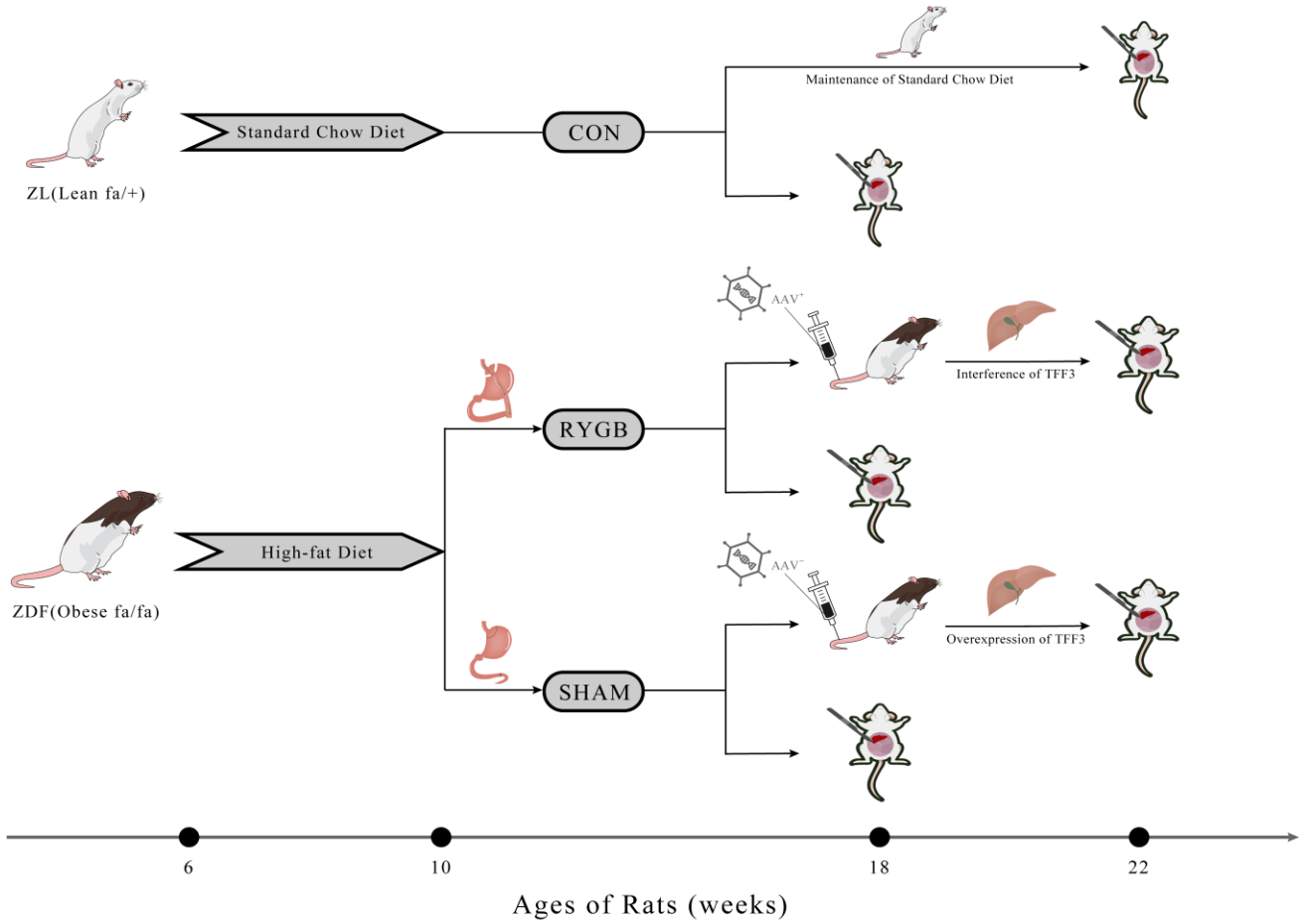


The expression of TFF3 in RYGB group was higher than that in sham group (Western blotting)



Whether TFF3 regulates blood glucose through PI3K-Akt pathway, and whether bariatric surgery plays a role in improving blood glucose by regulating liver TFF3 expression deserve further study

Research content



After 4 weeks of high fat diet, ZDF rats were divided into RYGB group (RYGB, n=12) and SHAM group (n=12), and underwent RYGB operation and sham operation, respectively

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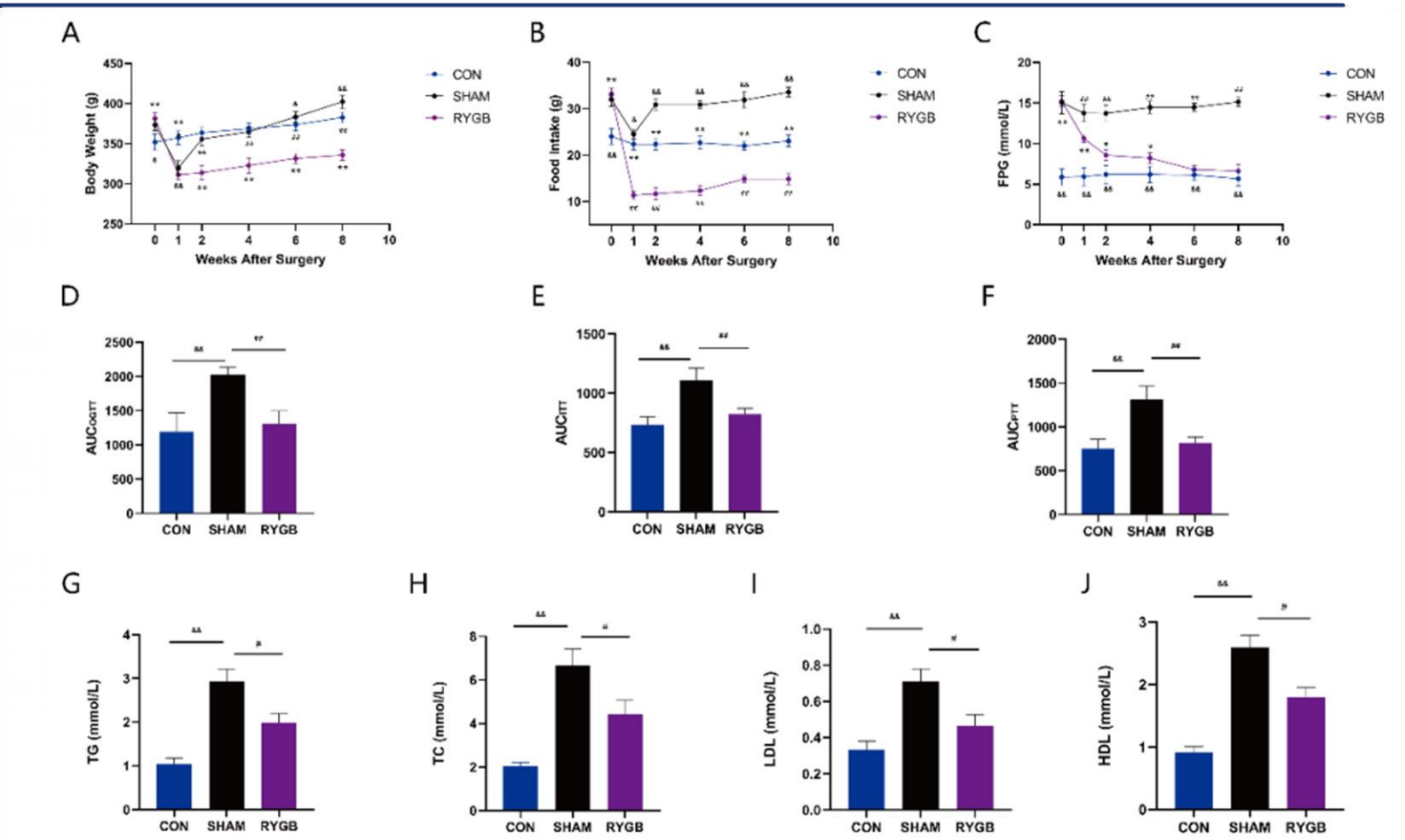

Effects of RYGB on body weight (Figure A), food intake (Figure B), blood glucose metabolism (Figure C) and serum biochemical parameters (Figure D-J) in ZDF rats

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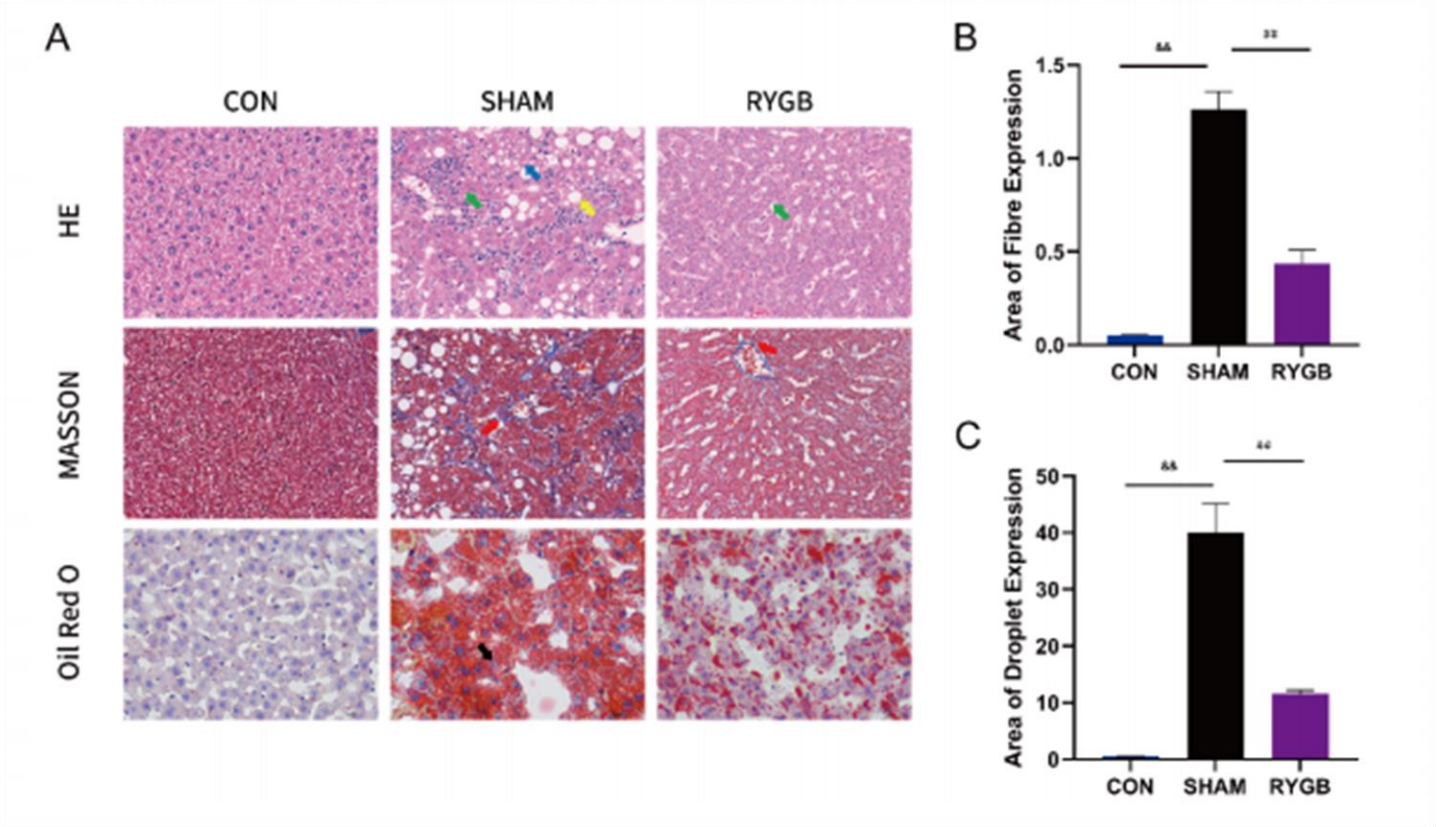
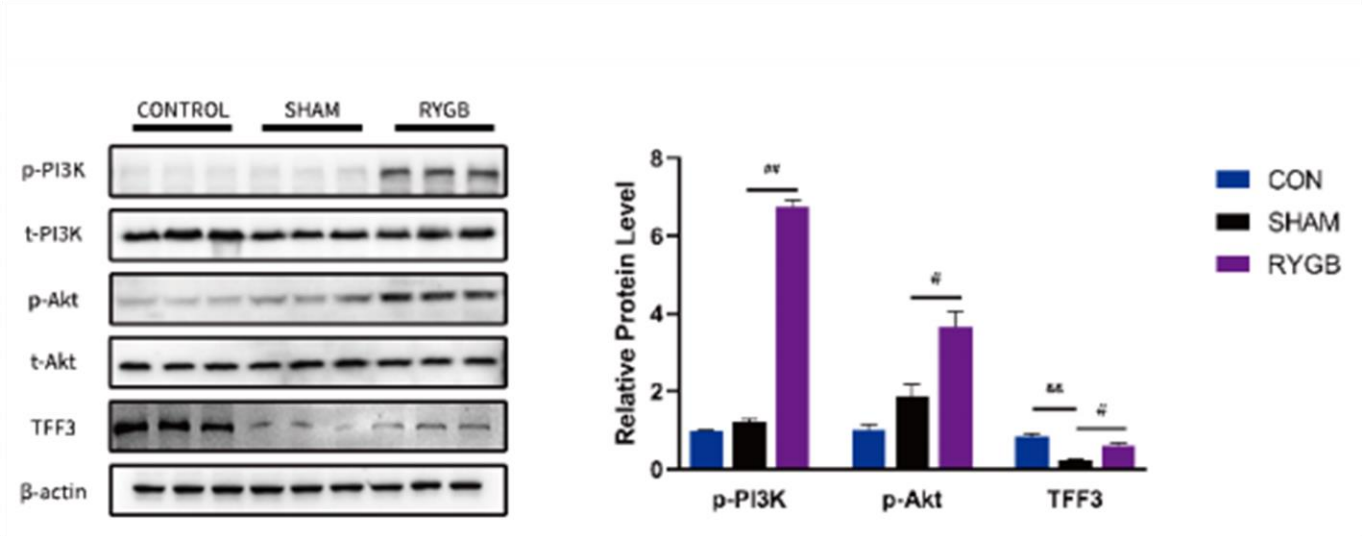


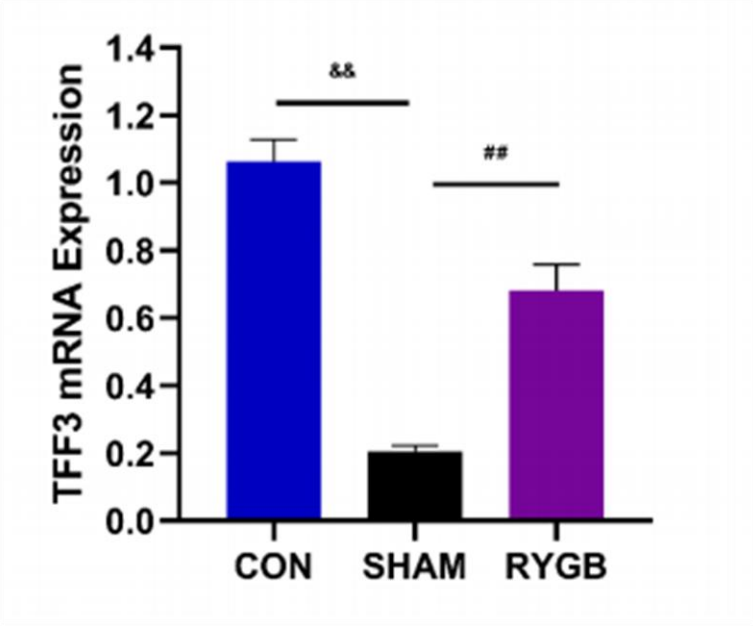
RYGB improves liver morphology and histopathology

Research content

Effects of RYGB on TFF3 and PI3K/Akt pathway activity in liver



Activation of PI3K /Akt pathway after RYGB is accompanied by upregulation of TFF3 and improvement of glucose metabolism



The expression level of TFF3 mRNA increased after RYGB

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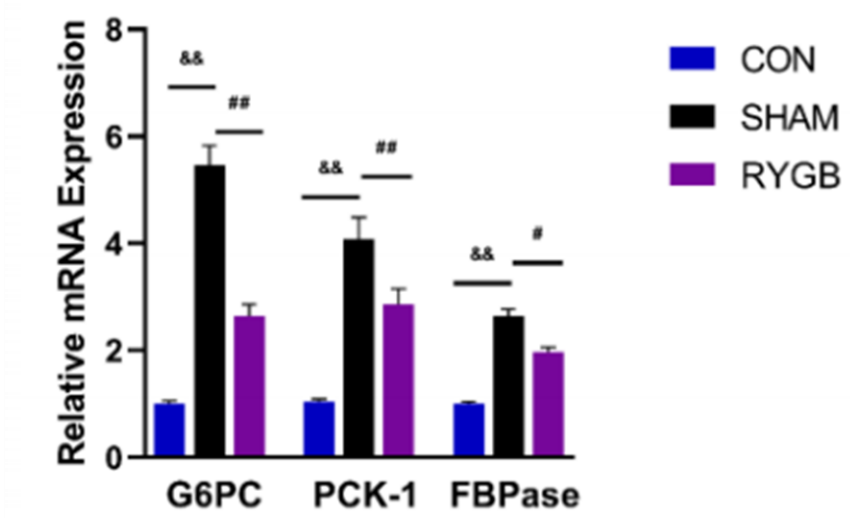
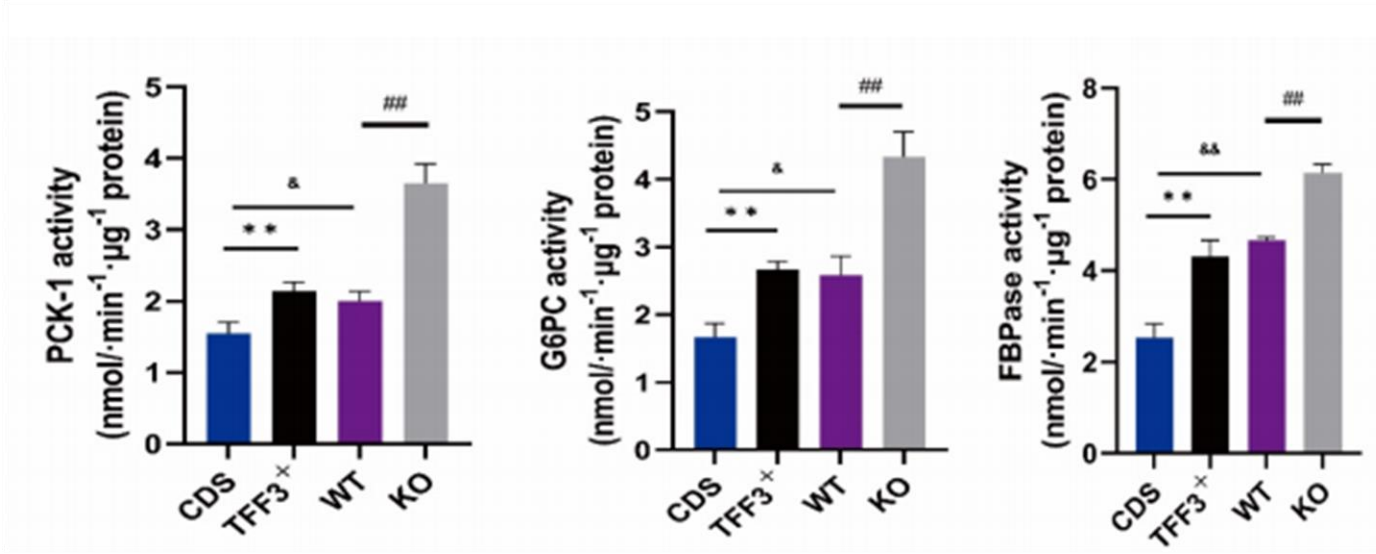
Effect of RYGB on enzymes of gluconeogenesis

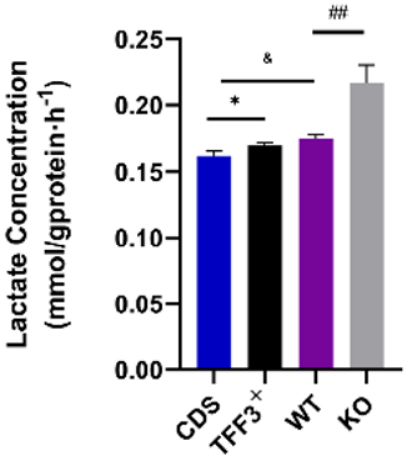


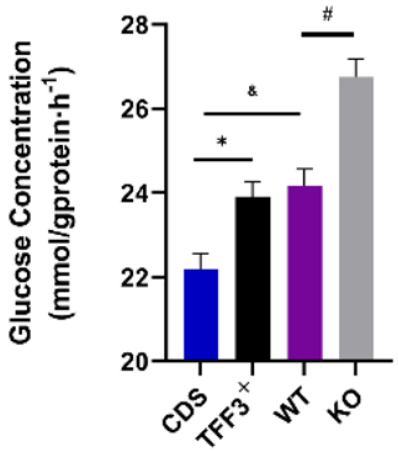
The activity of gluconeogenic enzymes in the RYGB group was lower than that in the sham operation group.



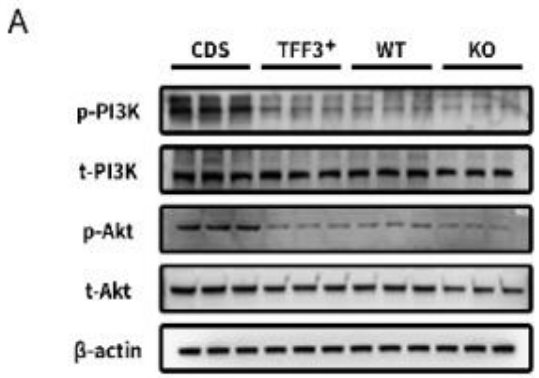
In vitro experiments showed that TFF3 overexpressing cell lines (CDS) showed lower gluconeogenic enzyme activity.

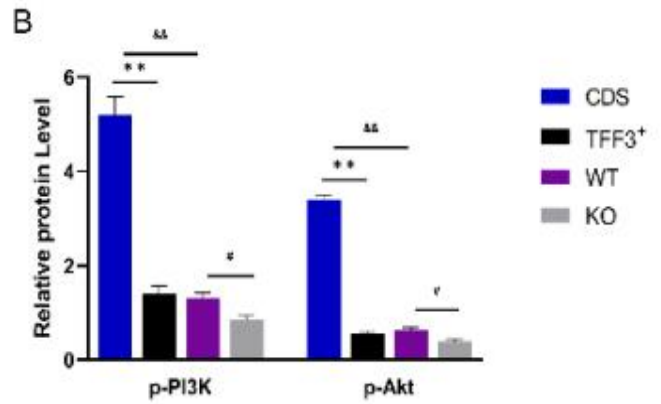
Research content





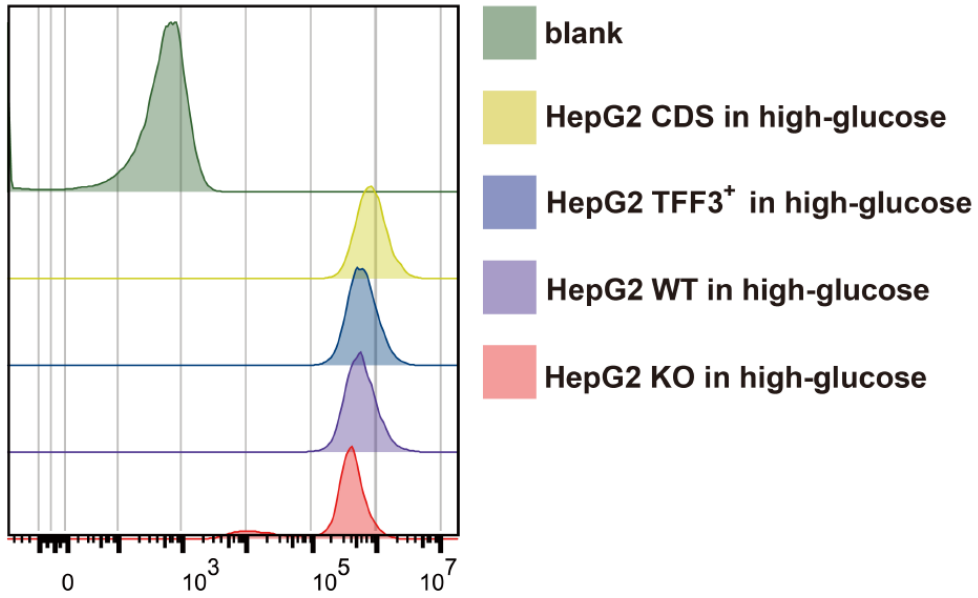
TFF3 knockout HepG2 cell lines showed higher lactate and glucose concentrations

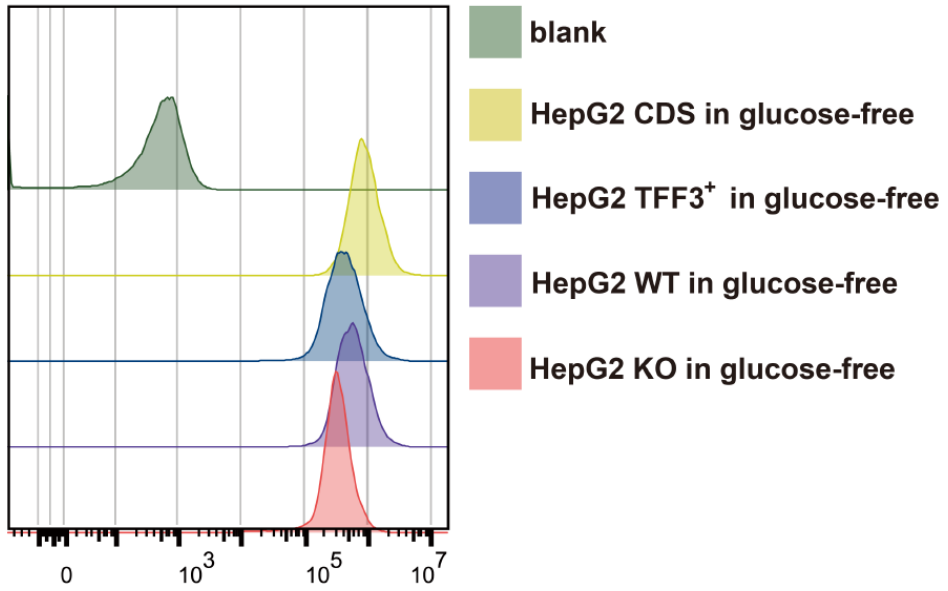




CDS cell lines overexpressing TFF3 have higher PI3K akt activity

Research content





In both high-glucose and glucose-free environments, CDS cell line has the strongest glucose uptake capacity

Results and discussion

Our study showed that RYGB significantly improved type 2 diabetes and lipid metabolism abnormalities in ZDF rats. It is most likely mediated by activation of the TFF3/PI3K/Akt signaling pathway, which regulates the activity of key gluconeogenic enzymes and enhances glucose uptake. In addition, the development of drugs targeting the regulation of TFF3 expression or PI3K/Akt activity based on the liver TFF3/PI3K/Akt pathway has clinical application potential.

THANKS A LOT!

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