CRISPR/Cas9-induced LEAP2 and GHSR1a knockout mutant zebrafish displayed abnormal growth and impaired lipid metabolism

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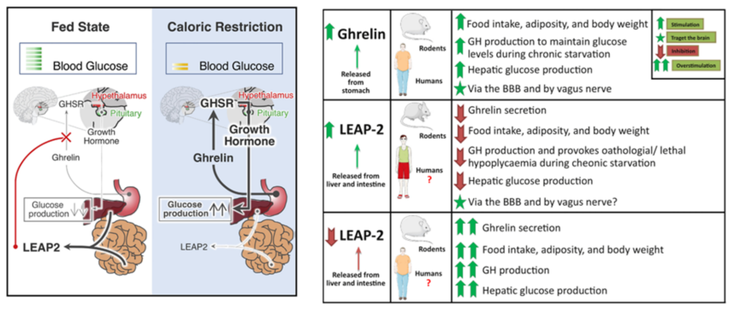
Introduction



1. Liver-expressed antimicrobial peptide 2 (LEAP2), originally described as an antimicrobial peptide, has recently been recognized as another ligand of growth hormone secretagogue receptor 1a (GHSR1a).
2. LEAP2, acts both as an endogenous competitive antagonist of ghrelin and an inverse agonist of constitutive GHSR1a activity, which vigorously blocks ghrelin's effects on food intake and energy metabolism in mice.

Methods

1. Construction of LEAP2 mutant strain of Zebrafish;
2. Effects of LEAP2 on appetite regulatory genes and swimming behavior;
3. Examination of growth indices and liver fat in adult zebrafish with LEAP2 mutation;
4. Construction of GHSR1a mutant of Zebrafish;
5. Examination of growth indices and liver fat in adult zebrafish with GHSR1a mutation;

Results

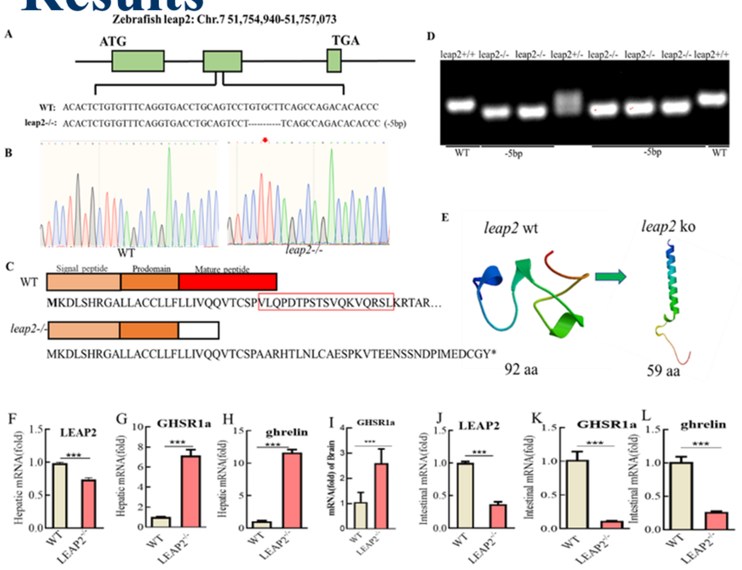


Fig 1 Establishment of zebrafish LEAP2 knockout strain and its regulation on the expression of LEAP2 and GHSR1a.

Results

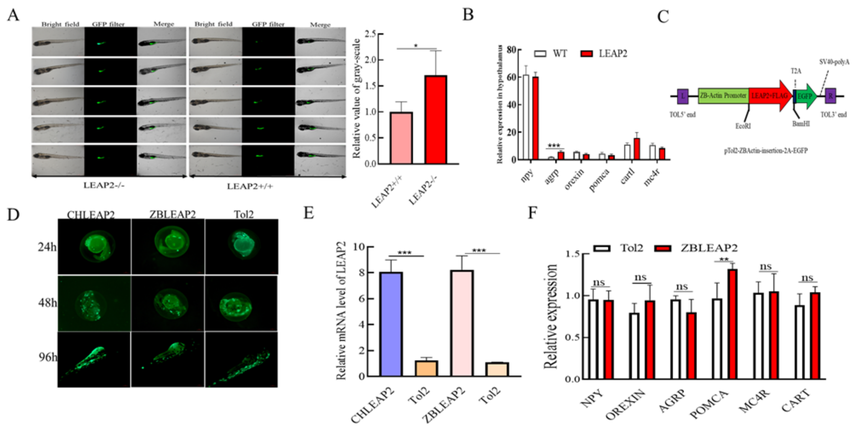


Fig 2. Expression regulation of food intake and appetite-related genes by LEAP2 in zebrafish larvae.

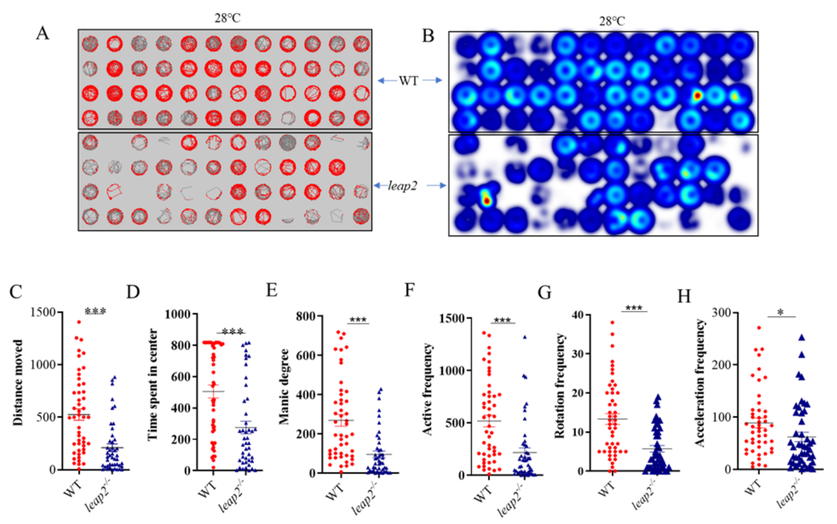


Fig 3. Effects of LEAP2$^{-/-}$ mutations on the locomotor activities of zebrafish larvae.

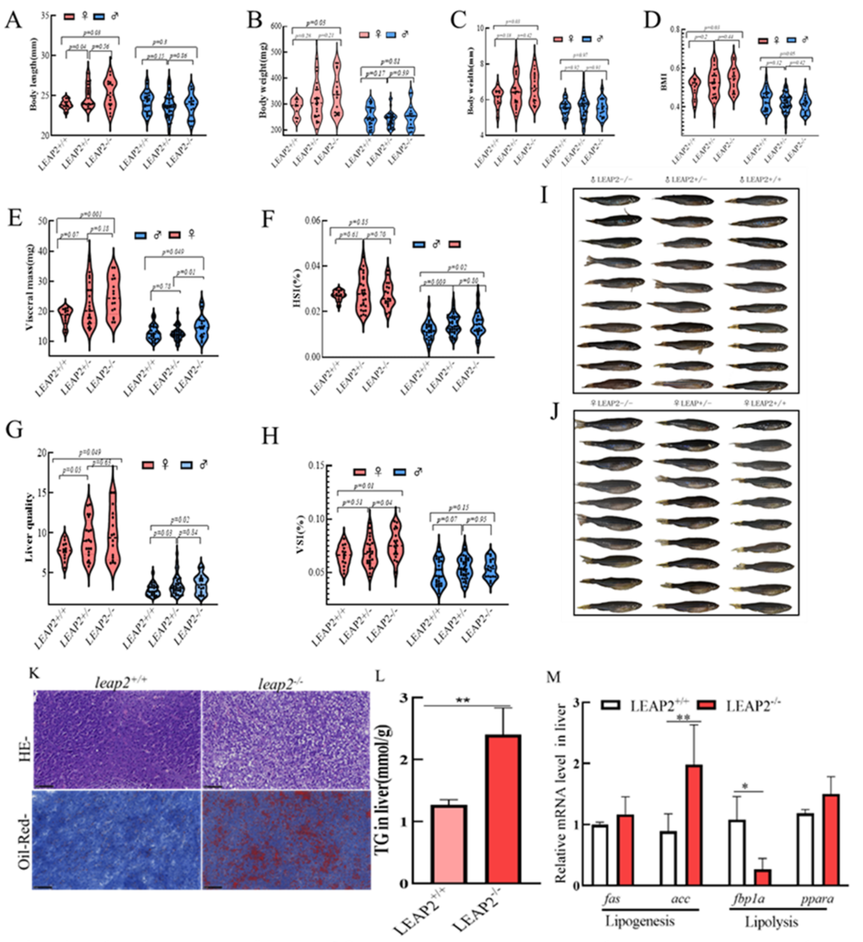


Fig 4. The impact of LEAP2 mutations on growth parameters and liver fat content in zebrafish.

Results

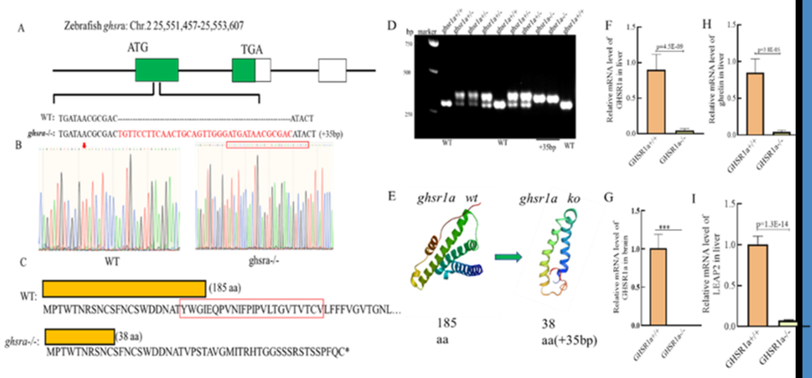


Fig 5. Zebrafish GHSR1a knockout and regulation of ghrelin and LEAP2 expression by mutations in GHSR1a$^{-/-}$.

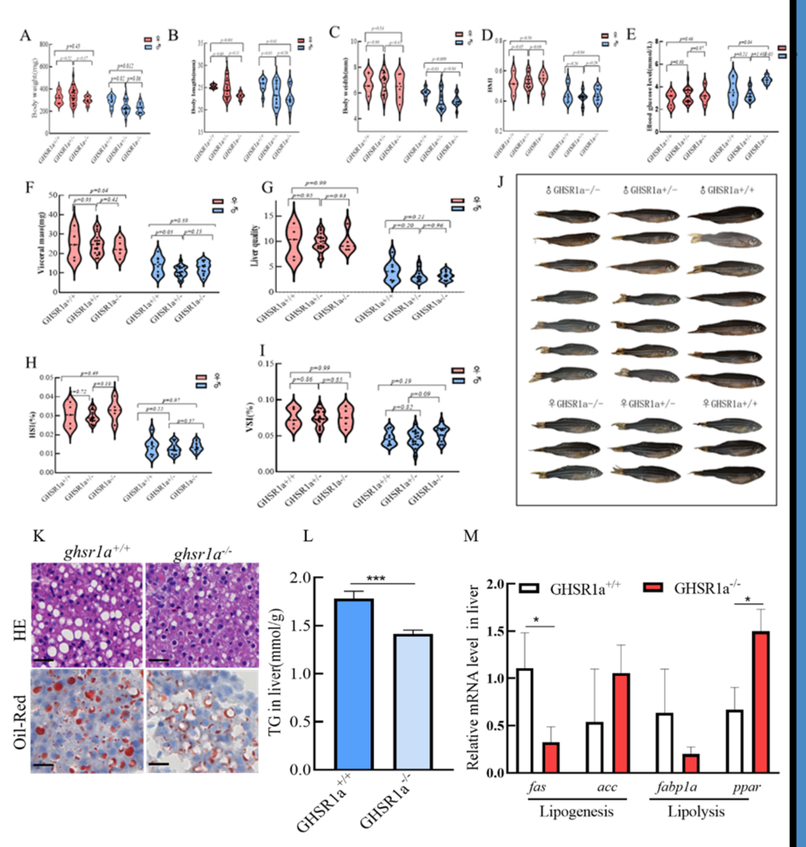


Fig 6. The effect of GHSR1a$^{-/-}$ mutations on growth parameters and hepatic lipid droplets in zebrafish.

conclusions

1.LEAP2 deficiency promotes high expression of liver ghrelin and brain GHSR1a.

2. LEAP2 deficiency leads to increase feeding and increased liver fat in zebrafish, resulting in obesity in female zebrafish.

3. Overexpression of LEAP2 leads to high expression of the appetite-suppressing factor POMC.

4. Loss of GHSR1a results in male zebrafish becoming leaner.

5. These research findings underscore the significance of LEAP2 as a satiety factor in the regulation of organismal energy balance, revealing its pivotal role in energy metabolism regulation through interaction with GHSR1a.

Acknowledgements

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