A Novel Cholesterol-Responsive Hepatic tRNA-derived Small RNA

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BACKGROUND

Cholesterol homeostasis is essential for normal biological function, but imbalances can lead to severe conditions, including cardiovascular disease (CVD), atherosclerosis, and hepatic steatosis. Traditional regulators of lipid metabolism, such as SREBPs and microRNAs (miRNAs), have been well-studied. However, the role of transfer RNA-derived small RNAs (tsRNAs) in lipid metabolism has remained largely understudied given that they are crucial players in diverse biological processes.

BRIEF DESCRIPTION

Prof. Changcheng Zhou and colleagues from the University of California, Riverside (UCR) have developed an antisense oligonucleotide to knockdown tsRNA-Glu-CTC, which is an abundant tsRNA in the liver and a critical regulator of cholesterol homeostasis. This specific tsRNA is cholesterol responsive and interacts with the master lipid regulator SREBP2. In vivo studies in mice demonstrated that the treatment reduces hypercholesterolemia and hepatic steatosis (fatty liver) in mice fed a high-cholesterol diet. This treatment is advantageous because it may open new therapeutic avenues for cardiometabolic conditions and liver disease.

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OTHER INFORMATION

KEYWORDS

tsRNA-Glu-CTC, ASO, cholesterol homeostasis, atherosclerosis, hypercholesterolemia, SREBP2, hepatic steatosis, cardiometabolic disease.

CATEGORIZED AS

- **Medical**
  - Disease: Cardiovascular and Circulatory System
  - Disease: Metabolic/Endocrinology

RELATED CASES

2025-662-0

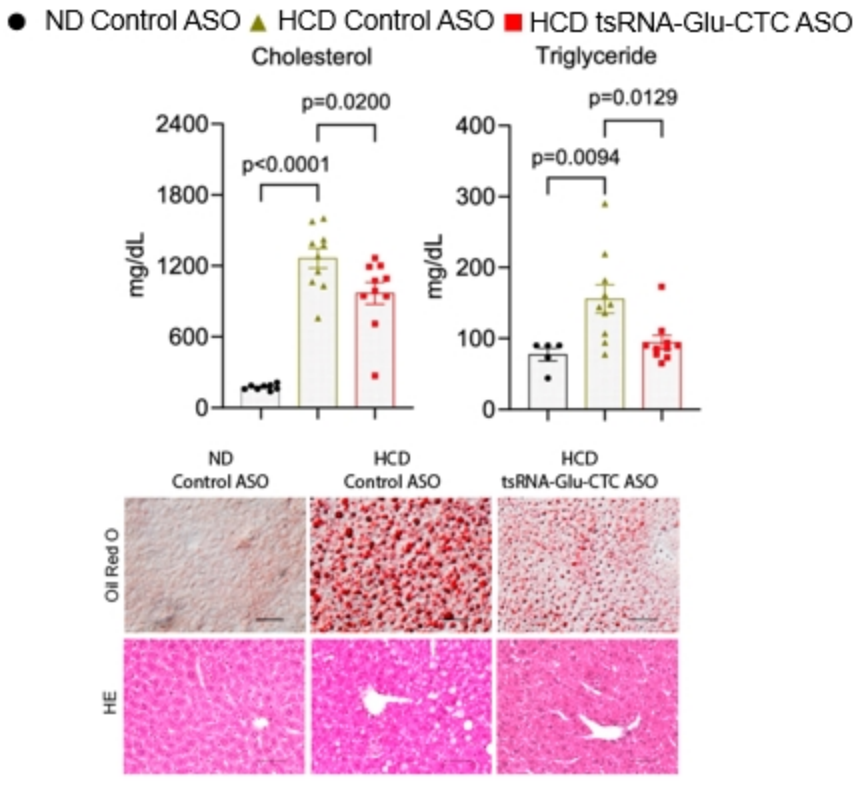


Fig 1: The reduction of serum cholesterol and triglyceride (top) and hepatic steatosis (bottom) with the UCR tsRNA versus the baseline (vehicle) and a control oglio.

Seven-week-old male Ldl receptor-deficient (Ldlr-/-) mice were fed a normal diet (ND) or high-cholesterol diet (HCD) and treated with tsRNA-Glu-CTC antisense oligonucleotides (ASO) or control ASO twice per week for 7 weeks.

SUGGESTED USES

▶ A potential cardiometabolic therapeutic treatment for a variety of conditions including atherogenic dyslipidemia (hypercholesterolemia and atherosclerosis) and metabolic liver disease (hepatic steatosis and fibrosis).

PATENT STATUS

Patent Pending

RELATED MATERIALS

▶ Li, X., Hernandez, R., Zhang, X. et al. A cholesterol-responsive hepatic tRNA-derived small RNA regulates cholesterol homeostasis and atherosclerosis development. Nat Commun 16, 11043 (2025). https://doi.org/10.1038/s41467-025-67387-z - 12/15/2025

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