**BACKGROUND**

Fatty liver disease (FLD), often caused by high-fat diets, is a major health concern. This study investigates:

- The role of fatty acid oxidative metabolism in FLD
- Potential of other fatty acid metabolism pathways as therapeutic targets for FLD

**RESULTS**

**Liver weight:**

- Increased in CactLiv-/- FLD group

**Gene expression changes:**

- CactLiv-/- mice:
  - ↑ Gluconeogenesis, mitochondrial/peroxisomal fatty acid oxidation, carnitine synthesis, ketogenesis
  - ↑ Pparα (lipogenesis)
  - ↓ Gluconeogenesis, carnitine synthesis, most mitochondrial fatty acid oxidation genes (except cpt1a)

**Control FLD mice:**

- ↓ Mitochondrial fatty acid oxidation, ketogenesis, systemic metabolism, peroxisomal fatty acid oxidation

**Acetyl CoA-carboxylase (AcAc) knockout / fatty liver diet (CactLiv)**

**Potential of other fatty acid catabolism pathways**

**Control genotype / control diet (Control) (n=5)**

**HYPOTHESIS**

We hypothesize that mitochondrial fatty acid oxidation is crucial in FLD pathogenesis. Knocking out the CACT gene in mice will result in more severe FLD progression on a high-fat diet compared to controls, with consistent molecular markers of mitochondrial and peroxisomal dysfunction.

**MATERIALS & METHODS**

**Gene Knockout**

- CACT knockout mice were compared to wild-type C57BL/6J controls.

**Fatty Liver Diet Regimen**

Mice were divided into four groups:

- Control genotype / control diet (Control) (n=5)
- Control genotype / fatty liver diet (CactLiv) (n=5)
- CACT knockout / control diet (Control-FLD) (n=5)
- CACT knockout / fatty liver diet (CactLiv-/-FLD) (n=5)

Control diet: standard chow (10 kcal% fat)

Fatty liver diet: high-fat (60 kcal% fat) for 7 days

**Data Analysis**

- Quantitative real-time PCR with SYBR Green on QuantStudio 6 Flex
- Primers for mitochondrial biogenesis, gluconeogenesis, fatty acid oxidation, ketogenesis, triacylglycerol synthesis
- E2M as housekeeping gene
- Samples run in duplicate with melt curve analysis for specificity

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**REFERENCES**


**CONCLUSION & DISCUSSION**

These findings suggest that mitochondrial fatty acid oxidation is crucial in protecting against FLD. CACT knockout impairs the liver’s adaptive response to a high-fat diet, and alternative fatty acid oxidation pathways may be activated as compensatory mechanisms. Further research is needed to explore potential therapeutic targets based on these findings.

**Next Steps:**

- Conduct a more comprehensive analysis of gene expression changes, possibly using RNA sequencing to identify additional pathways involved in the compensated response to CACT knockout.
- Perform metabolomic studies to better understand the alterations in lipid metabolism and identify potential biomarkers.
- Investigate the effects of pharmacological interventions that target the upregulated pathways identified in this study, such as peroxisomal fatty acid oxidation, in CACT knockout mice.

**Figures:**

- Fig. 1: Percentage Liver of Mice Total Body Weight (BW)
- Fig. 2: Gluconeogens
- Fig. 3: Mitochondria FAD
- Fig. 4: Peroxisomal FAD
- Fig. 6: Peroxisomal FAO