# Low dose thyroid hormone improves hepatic mitochondrial fatty acid oxidation and rescues nonalcoholic fatty liver disease in mice

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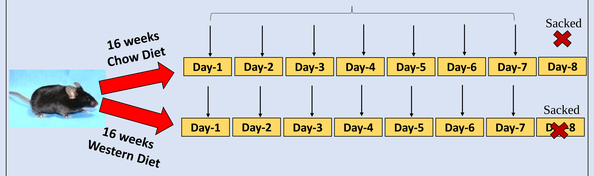
## INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is an umbrella term covering for illnesses characterized by excessive fat accumulation in the liver that aren't caused by alcohol consumption. In the United States, NAFLD is the most common chronic liver disease, affecting about 20-40% of the population.[1,2] Mitochondrial trifunctional protein (MTP) is a complex enzyme made up of 4α and 4β subunits that catalyzes the last three steps of fatty acid β-oxidation.[3] Mitophagy, a sort of mitochondrial quality control, has recently been shown to play a key role in the development of NAFLD. Thyroid hormone (TH) is an important regulator of lipid metabolism and may have the potential to treat NAFLD, but its use is associated with adverse systemic effects. It's unclear whether improving mitochondrial fatty acid oxidation (FAO) can help people with NAFLD.

## AIM

To study whether low dose TH improves mitochondrial FAO and mitochondrial biogenesis/mitophagy in mice and thereby helps them recover from NAFLD.

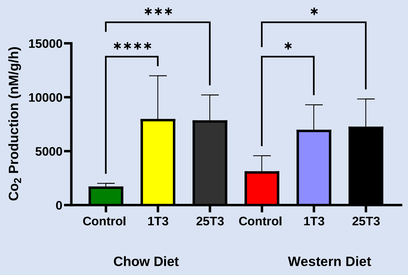
## METHOD



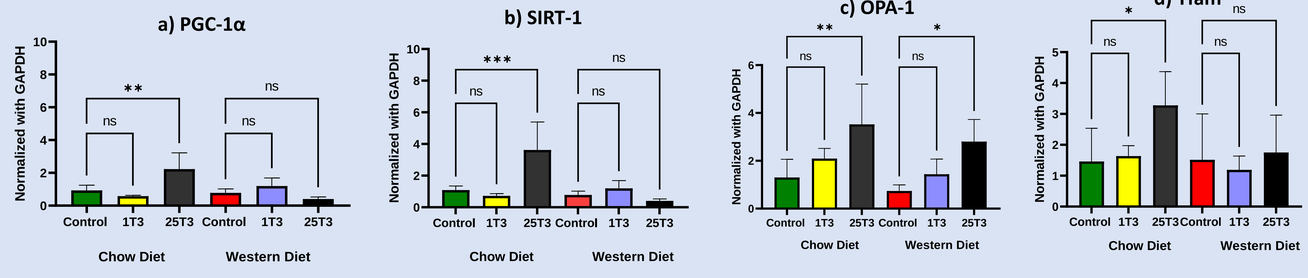

| Diet | No of animals used (n) | Control (PBS) | T3 (1µg/100g b.w) | T3 (25µg/100g b.w) |
|---|---|---|---|---|
| Chow | 8 per group | 7 days | 7 days | 7 days |
| Western | 6 per group | 7 days | 7 days | 7 days |

## RESULTS

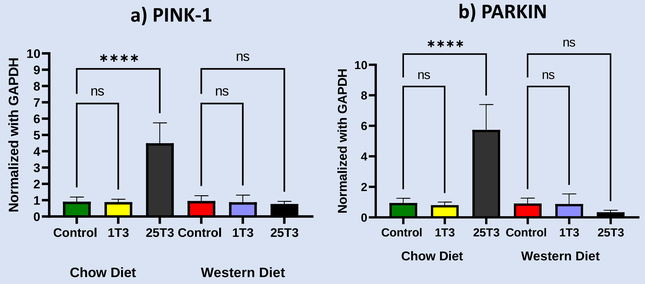
### Fig. 1 Hepatic Fatty Acid Oxidation



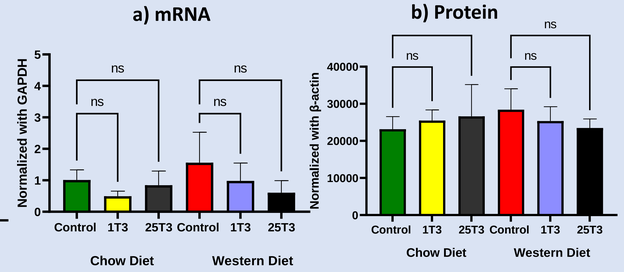

### Fig. 2 Hepatic Mitochondrial Biogenesis Markers



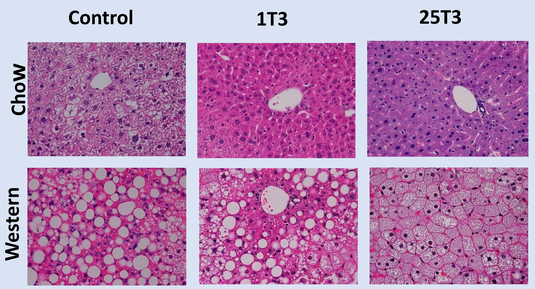

### Fig. 3 Mitophagy Markers




### Fig. 4 Hepatic MTP RNA and Protein Expression




### Fig. 5 Histology




Values are presented as Mean ± S.D. * p<0.05; ** p<0.01. *** p<0.001; **** p<0.0001; NS – Not Significant.

## TABLE-1: SERUM BIOMARKERS

| Parameter | Diet | Control | 1T3 | 25T3 |
|---|---|---|---|---|
| ALT | Chow | 42.50 ± 15.38 | 38.75 ± 2.38 | 56.75 ± 6.49 |
| | Western | 387.00 ± 15.38 | 177.01 ± 11.64 ** | 168.75 ± 9.74 ** |
| Cholesterol | Chow | 98.01 ± 15.85 | 62.66 ± 15.45 | 39.83 ± 21.48 * |
| | Western | 223.50 ± 59.74 | 157.75 ± 37.07 * | 91.60 ± 11.65 *** |

* : Control compared to 1T3 and 25T3

## CONCLUSIONS

- TH rescues NAFLD in mice by increasing hepatic FAO and mitochondrial biogenesis and mitophagy markers.
- TH increases hepatic FAO without increasing MTP expression but with improving mitophagy and biogenesis.
- This study suggests that low dose thyroid hormone is a potential treatment modality for NAFLD.

## REFERENCES

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