Investigating the Effects of Diet on Hepatic Gene Expression

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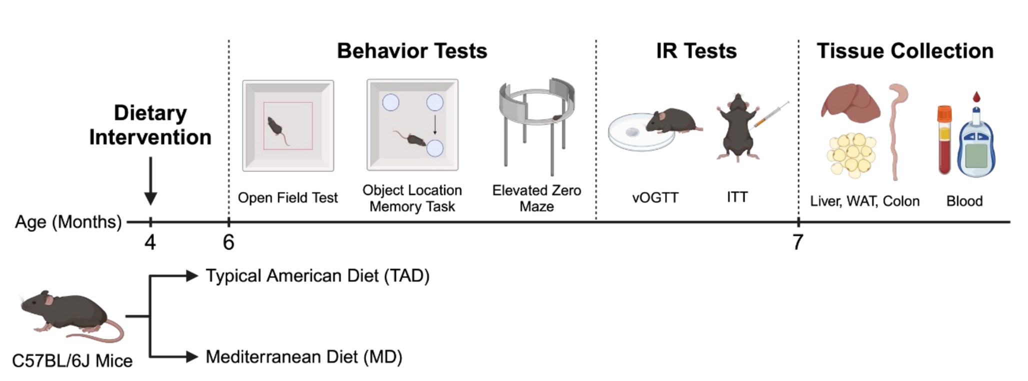
Metabolic dysfunction-associated fatty liver disease (MAFLD) is a growing health concern, affecting nearly 24% of U.S. adults. It is characterized by excessive fat accumulation in the liver, and is linked to obesity, insulin resistance, and poor dietary habits. Oxidative stress plays a key role in disease progression, with excessive saturated fat intake exacerbating liver damage. Genes involved in lipid metabolism and oxidative stress will influence lipid storage and antioxidant defenses and may be influenced by diet. Our study investigates the effects of two diets; the Typical American Diet (TAD) which is high in saturated fats, and the Mediterranean Diet (MED) rich in unsaturated fats, on liver health. Findings suggest that diet influences gene expression, affecting both lipid metabolism and oxidative stress pathways. Understanding these mechanisms may help develop dietary strategies for MAFLD prevention, emphasizing the role of nutrition in liver health.

Introduction

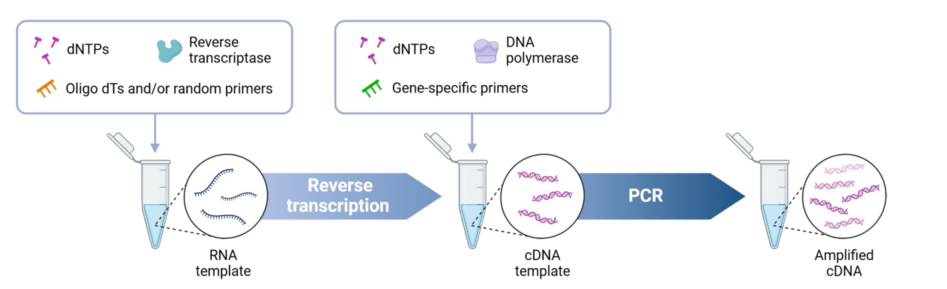
- Metabolic dysfunction-associated fatty liver disease (MAFLD) is characterized by fat accumulation in the liver in addition to metabolic imbalances
- Diet, genetics and lifestyle are risk factors for MAFLD
- The Mediterranean diet (MED) is rich in healthy fats and supports heart health and longevity.
- The Traditional American diet (TAD) is high in saturated fats and linked to inflammation and metabolic dysfunction
- MAFLD can lead to oxidative stress, lipid dysregulation and inflammation in the liver
- Nrf2 and Gpx1 are markers of oxidative stress
- Dgat2, Pparg, and Srepb1 are lipid metabolism genes
- Diet influences MAFLD disease progression

Methods



Diet	Typical American Diet (TAD)	Mediterranean Diet (MED)
Fat Source (35%)	Safflower oil, beef fat	Olive oil, fish oil
Protein Source (15%)	Casein (milk fat)	Egg whites, fish protein
Carbohydrates (50%)	Corn starch	Brown rice & wheat starch
Associated with	Obesity, hypertension	Longevity, heart health

Two-step RT-PCR



Results

Lipid Metabolism Gene Expression

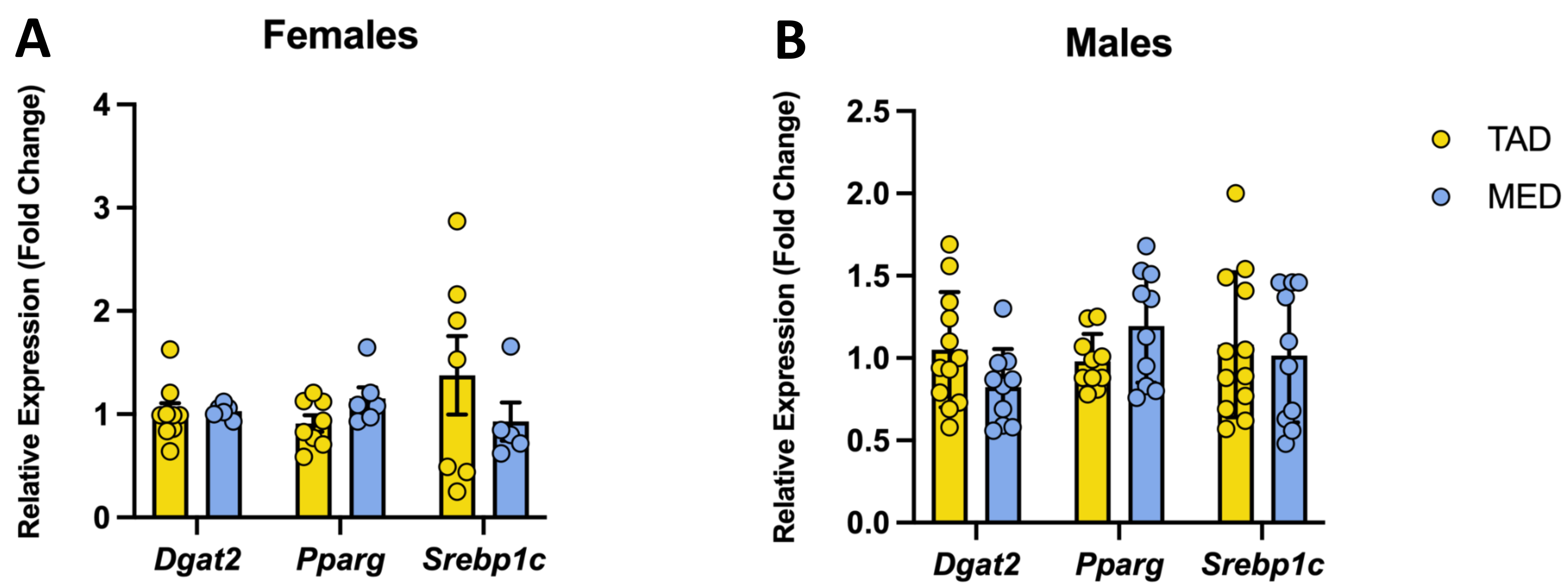


Figure 1. Diet-induced lipid metabolism gene expression. Unpaired t-tests revealed no significant difference in relative expression of *Dgat2*, *Pparg*, or *Srebp1c* between the MED and TAD diets for both females (A) and males (B).

Oxidative Stress Gene Expression

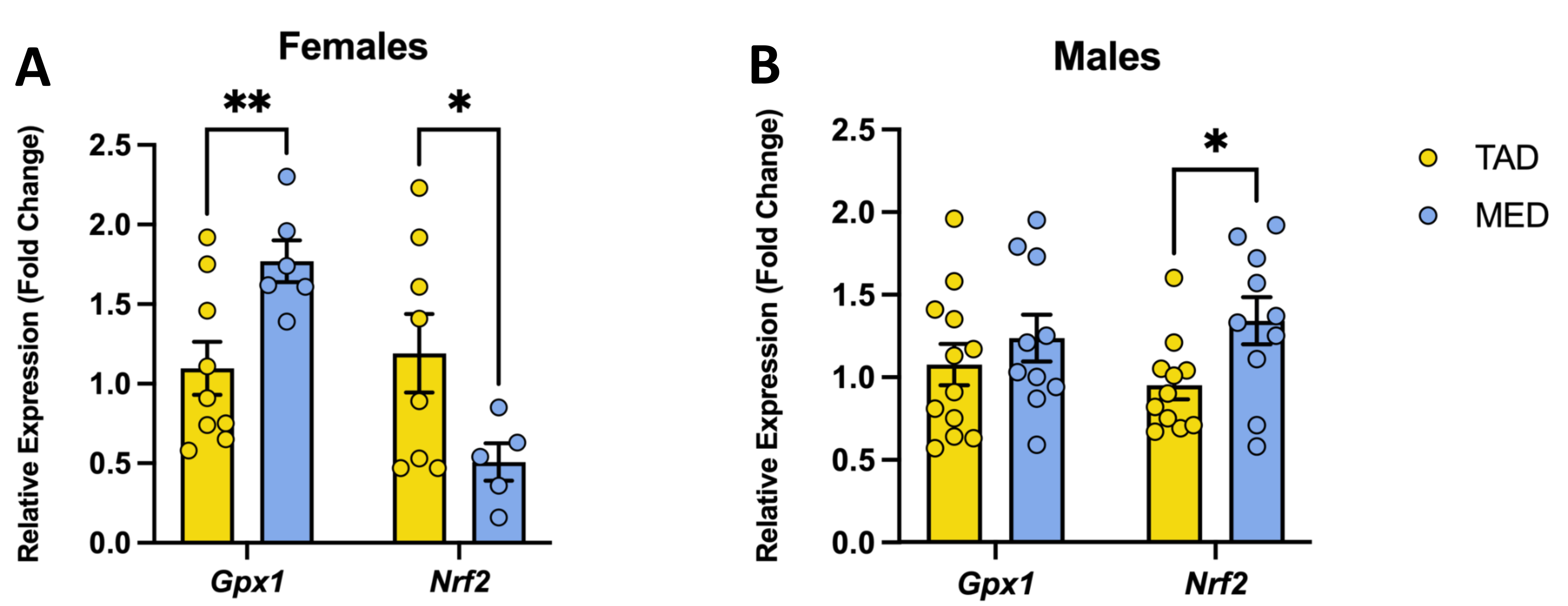
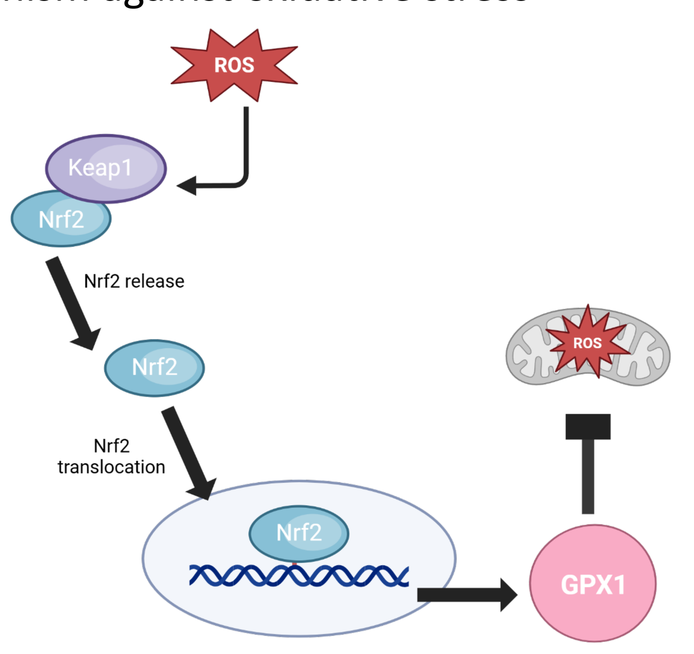


Figure 2. Diet- induced oxidative stress gene expression. Unpaired t-tests revealed significant difference in gene expression levels of *Gpx1* and *Nrf2* in females (A), significant difference in gene expression of Nrf2 but no significant difference in gene expression of *Gpx1* in males (B).

Conclusions

- Males on MED diet have increased requirement for *Nrf2*
- Females rely on estrogen and *Gpx1* as a protective mechanism against oxidative stress



Future Directions

- Extend diet duration to 6 or more months
- Test other gene markers of oxidative stress
- Investigate actual levels of oxidative damage in tissues to look at overall tissue function
- Explore estrogen's protective role against oxidative stress

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