Effects of Parental Diet on the Offspring's Epigenome and Expression of Genes Associated With Alzheimer's Disease

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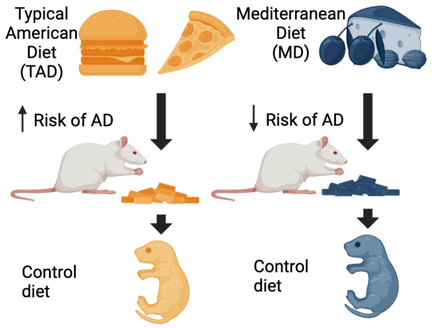
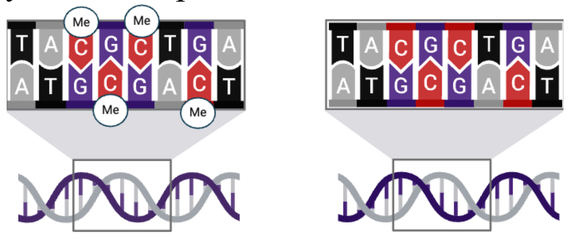
Background

- **Alzheimer's disease (AD):** a severe neurodegenerative disease known to cause dementia.
- Research in mice suggests parental diet affects the risk of offspring developing symptoms related to AD



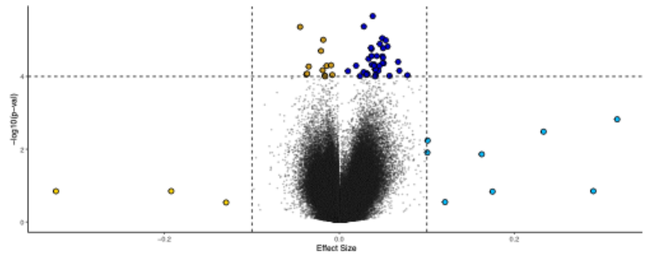
- Late-onset AD has a significant heritable component, but very few SNPs are associated with AD development
- **Epigenetic Alterations**: Changes to genome structure and gene activity that does *not* involve modifications to the DNA sequence, often occurring through chemical modifications like DNA methylation of cytosine at CpG sites



Hypermethylation ≈ ↓ Gene Expression

Hypomethylation ≈ ↑ Gene Expression

Diet-Driven Methylation



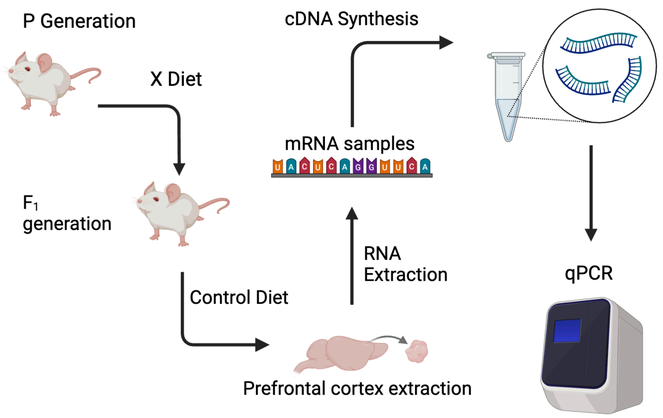
DML Type: MD Eff MD Sig TAD Eff TAD Sig

Figure 1. Volcano plot of DMLs based off of diet according to effect size (≥10%) and statistical significance (p-val≤0.0001).

Gaps in Knowledge/Objective

1) We understand there is a connection between parental diet and methylation.
2) However, we do not know if these differences are heritable and result in variation in gene expression in the F_1 generation.
3) Therefore, the goal of this study was to measure patterns of gene expression in genes related to AD in F_1 mice fed a control diet.

Methods



Gene Expression Results

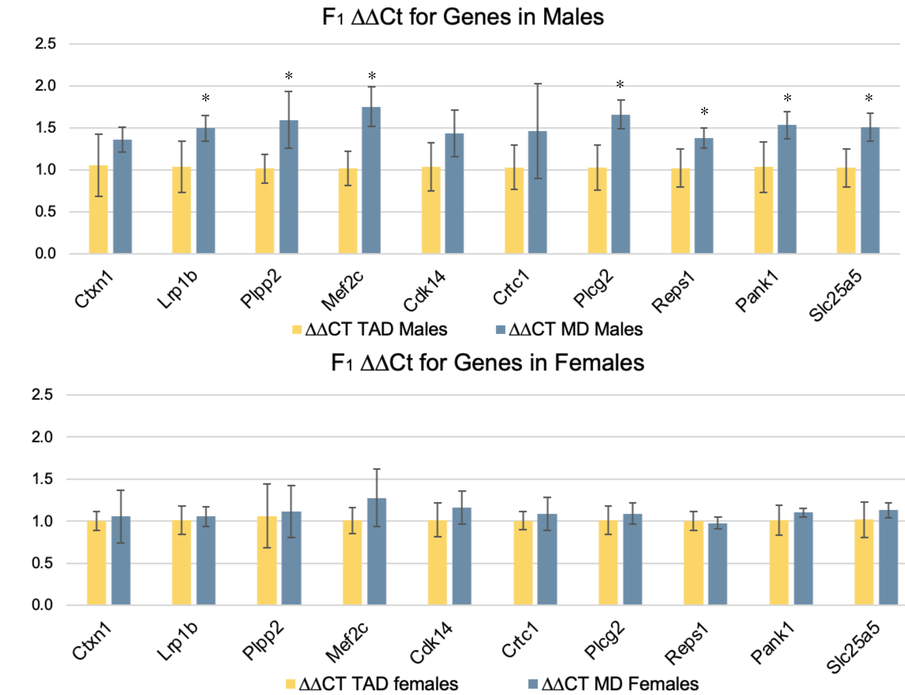


Figure 2. ΔΔCt scores for selected loci for offspring on either diet split by sex with TAD as the reference group. Significant differential expression, $p < 0.05$, is indicated by *

Conclusions and Future Studies

- Three out of four "effect size genes" were unregulated in MD offspring males as were four out of six "significant genes."
- No genes were differentially expressed between diets in females.
- Future studies should examine other epigenetic changes.
- Biochemically set female mice to menopause in future research.

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