

# MURINE ILEAL INTERPOSITION INDUCES SUBCUTANEOUS WHITE ADIPOSE TISSUE REMODELING WITH ENHANCED LIPOLYSIS, FATTY ACID OXIDATION, AND MITOCHONDRIAL TRANSPORT

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## Introduction

Metabolic surgery improves obesity-associated disease through both weight-dependent and weight-independent mechanisms. However, the peripheral metabolic pathways driving these benefits remain incompletely understood.

Ileal interposition (I-I) is a simplified metabolic operation that reproduces key metabolic effects of bariatric surgery **without gastric restriction or intestinal bypass**.

## Hypothesis

Ileal interposition induces transcriptional remodeling **of subcutaneous white adipose tissue (scWAT)** that contributes to systemic metabolic improvements.

## Methods

Male C57BL/6J mice (n=27) were maintained on high-fat (60% kcal) or low-fat (10% kcal) diets and randomized to ileal interposition or control groups.

Subcutaneous WAT was harvested 4 weeks post intervention and analyzed using **bulk RNA sequencing**.

Differential expression was modeled using **limma (R/Bioconductor)** across surgery and diet contrasts.

Significance threshold: **FDR ≤ 0.05**

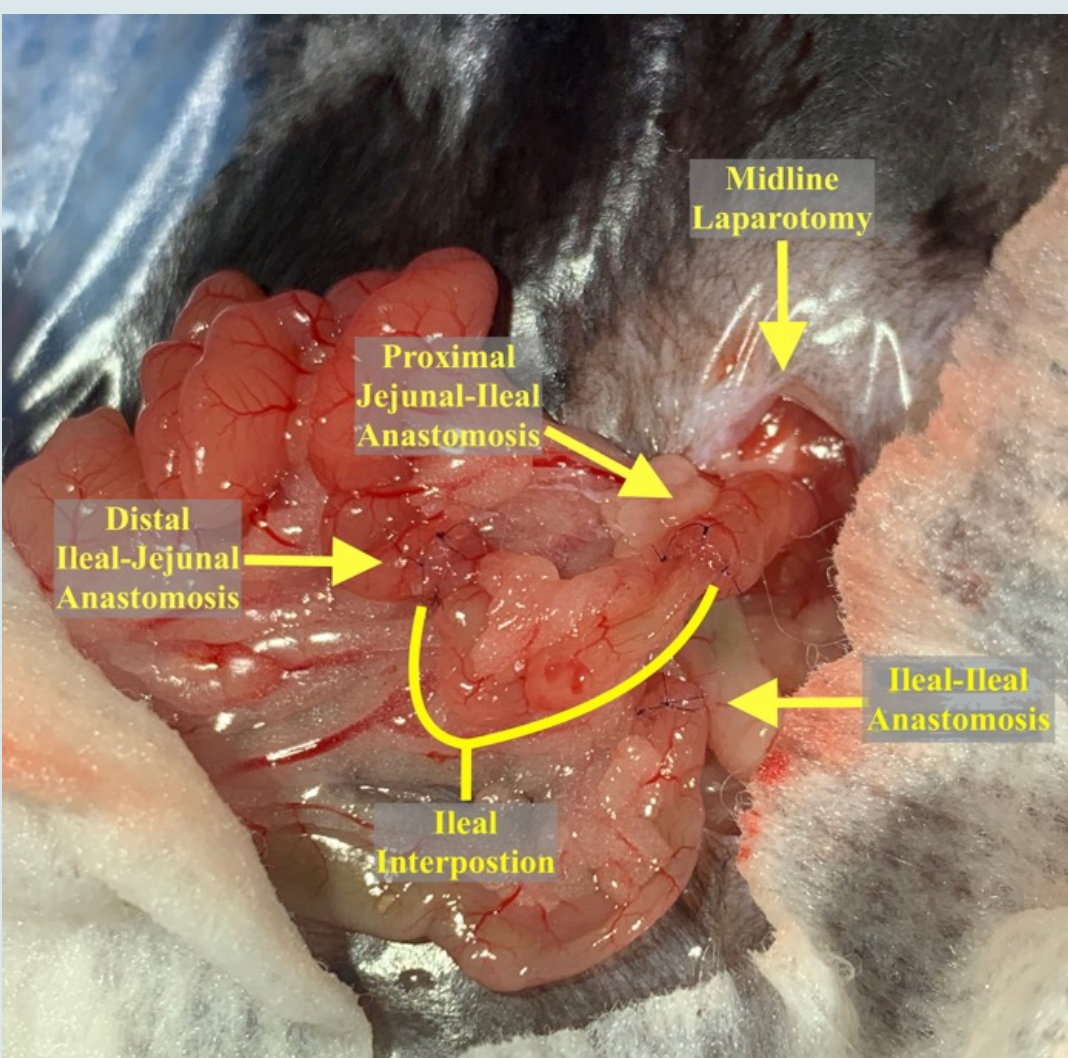


Figure 1. Ileal interposition surgical model.

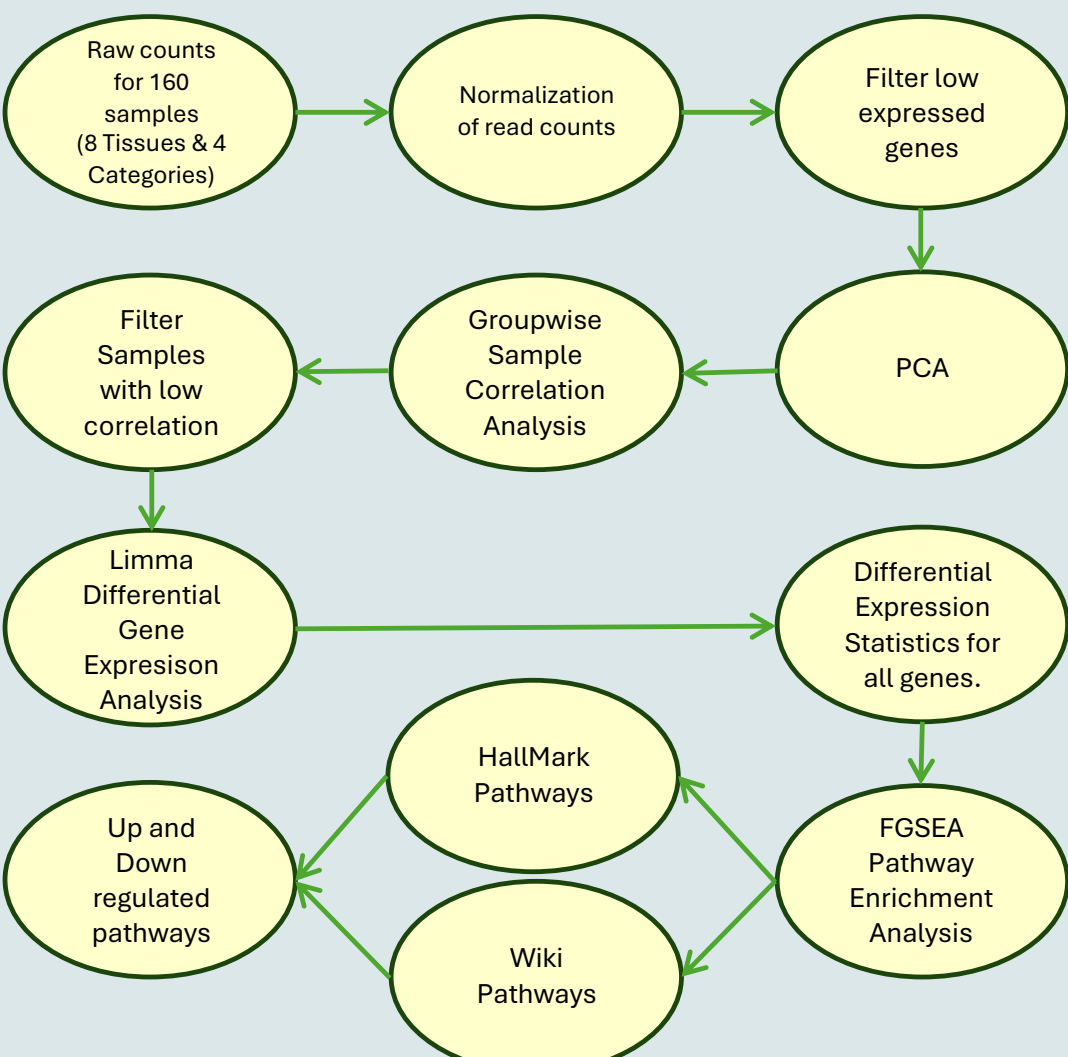


Figure 2 – RNA-seq analysis pipeline

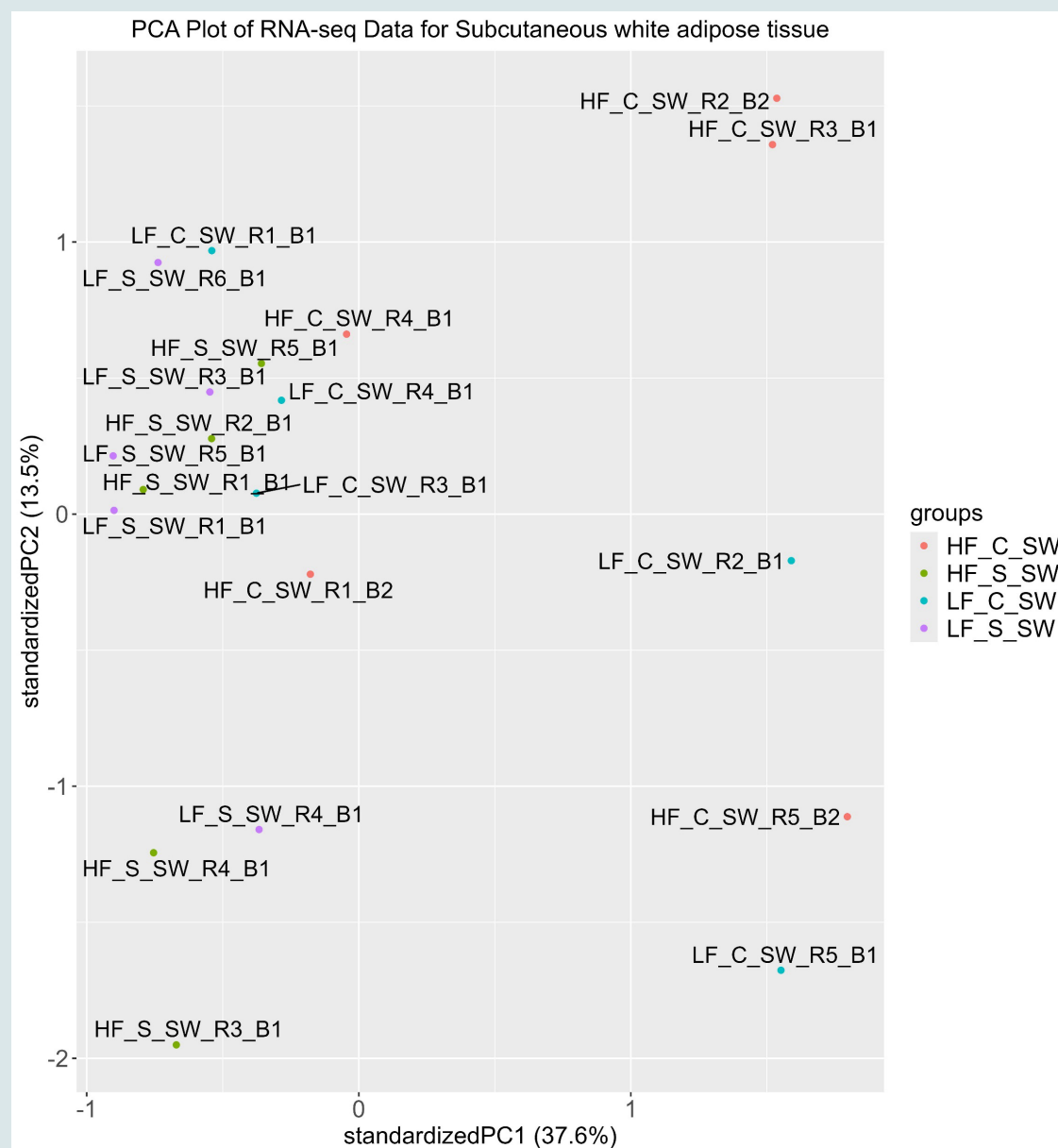


Figure 3 – PCA sample clustering

## Results

**382 genes** met concordance criteria across surgery comparisons.

**50 genes demonstrated consistent upregulation following ileal interposition** - Median log2 fold-change 0.76 (IQR 0.41) Range 0.32 - 2.19

| Magnitude of Response              | Fold Change | Genes (n) |
|------------------------------------|-------------|-----------|
| log <sub>2</sub> fold-change ≥0.58 | ≥1.5x       | <b>39</b> |
| log <sub>2</sub> fold-change ≥1    | ≥2x         | <b>13</b> |
| log <sub>2</sub> fold-change ≥2    | ≥4x         | <b>3</b>  |

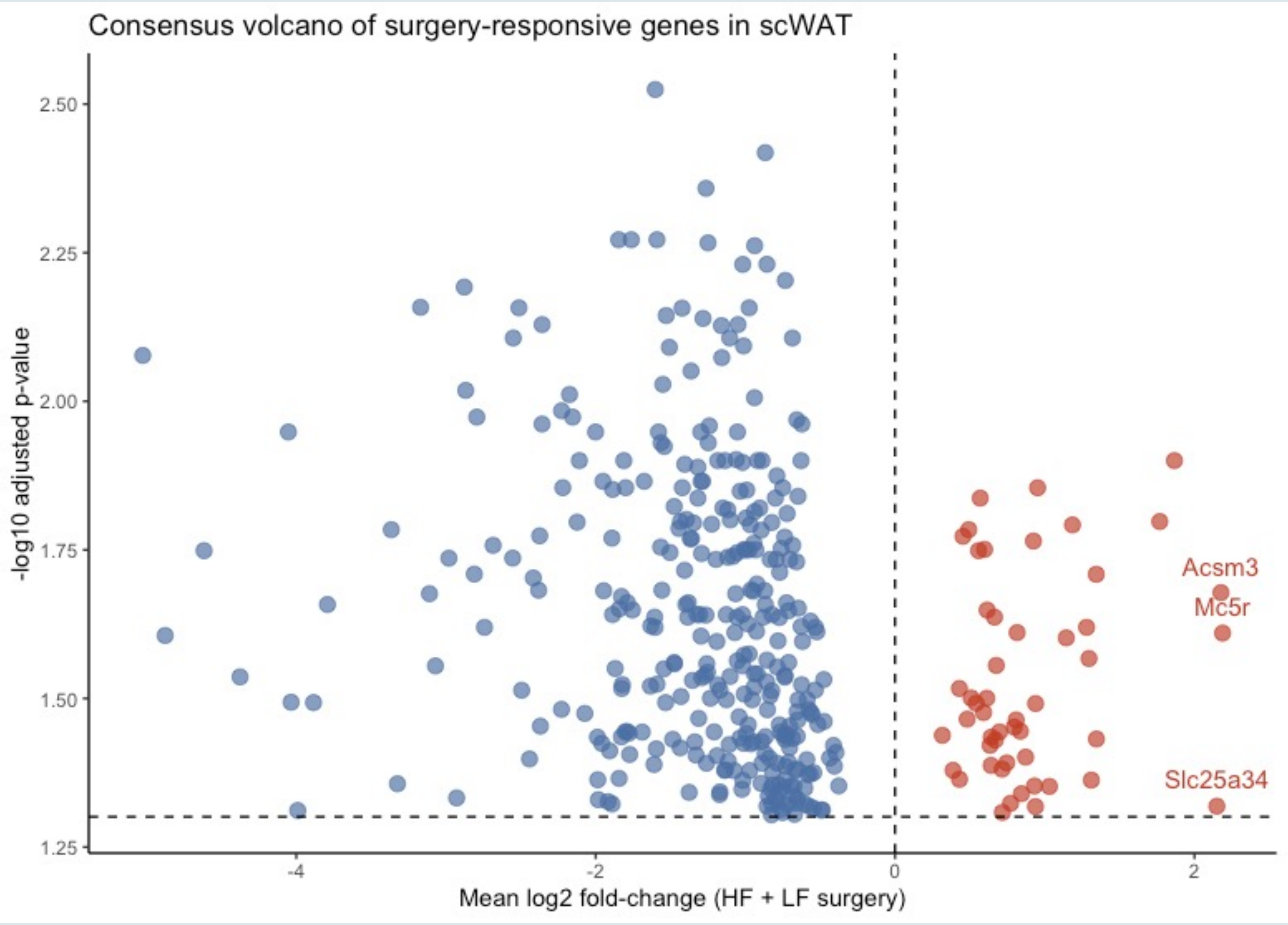


Figure 4 – Consensus volcano plot

## Key Genes Identified

- AcsM3** – fatty acid activation
- Mc5r** – regulator of lipolysis
- Slc25a34** – mitochondrial transport

## Biological Interpretation

Ileal interposition induces transcriptional reprogramming of scWAT characterized by:

- Increased lipolysis signaling
- Enhanced fatty acid activation
- Increased mitochondrial transport and metabolism

These transcriptional changes appear independent of dietary fat exposure, supporting an operation-driven metabolic effect.

## Proposed Mechanism

Gastrointestinal rearrangement may induce adipose remodeling through upstream gut-derived metabolic signals including:

- incretin hormones
- bile acids
- intestinal metabolic signaling pathways

These signals may coordinate cross-talk between:

- intestine
- liver
- adipose

Metabolic surgery **reprograms** peripheral adipose metabolism without restriction or malabsorption.

