Elucidating the Role of Endothelial Piezo1 on the Gut Microbiome in Mice

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INTRODUCTION

- Piezo1 is a cation channel known for its mechanosensing role in the endothelium.
- Piezo 1 has been found to play a role in microbial RNA sensing and serotonin production in the gut, as well as bile acid metabolism.
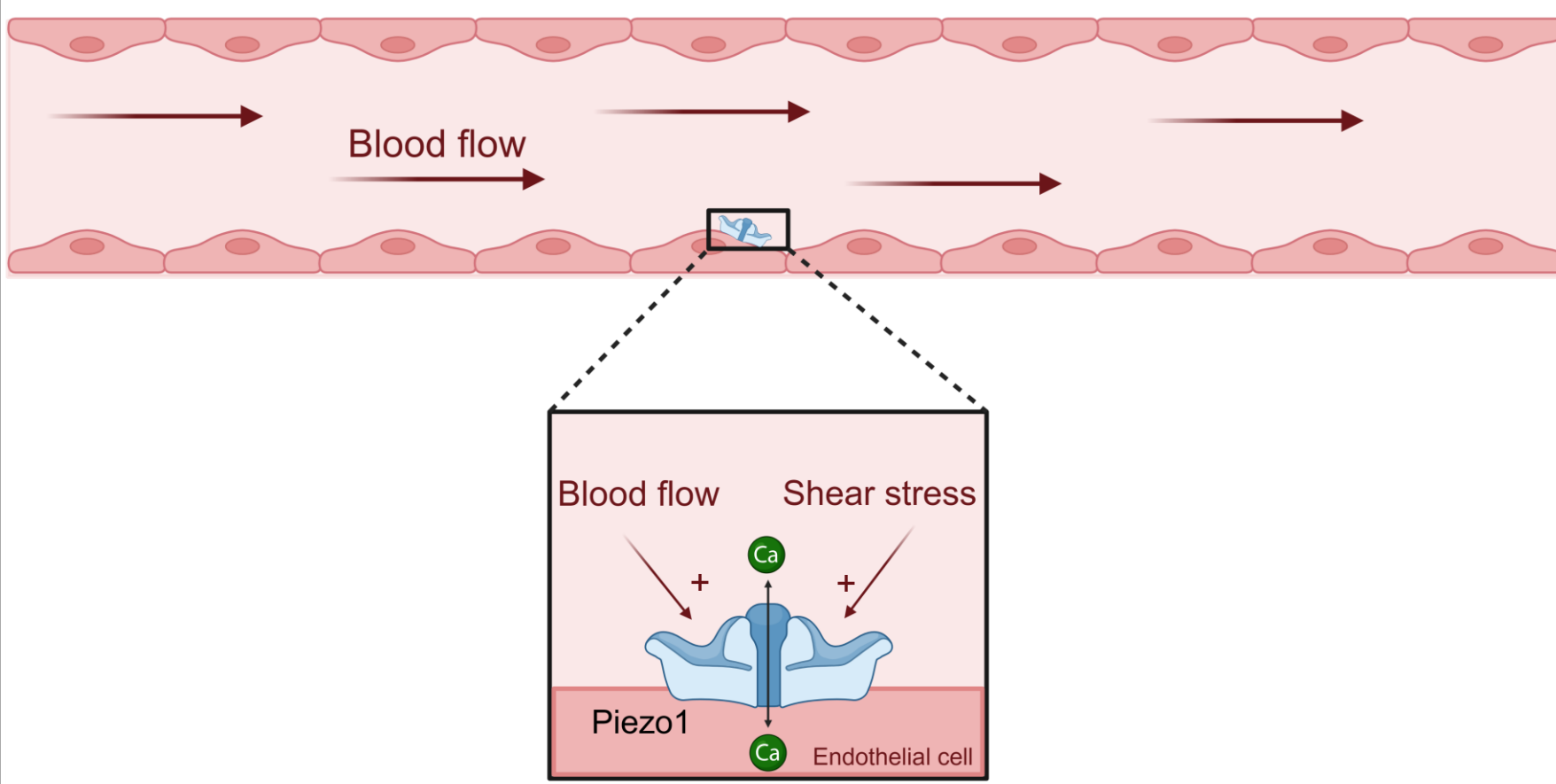

Figure 1. Illustration of Piezo1 stimuli (blood flow and sheer stress) and its location in endothelial cells. Created with BioRender.com

STUDY AIM

This study aimed to elucidate the impact of endothelial Piezo1 on gut microbiome diversity and composition upon high dietary fat intake in mice.
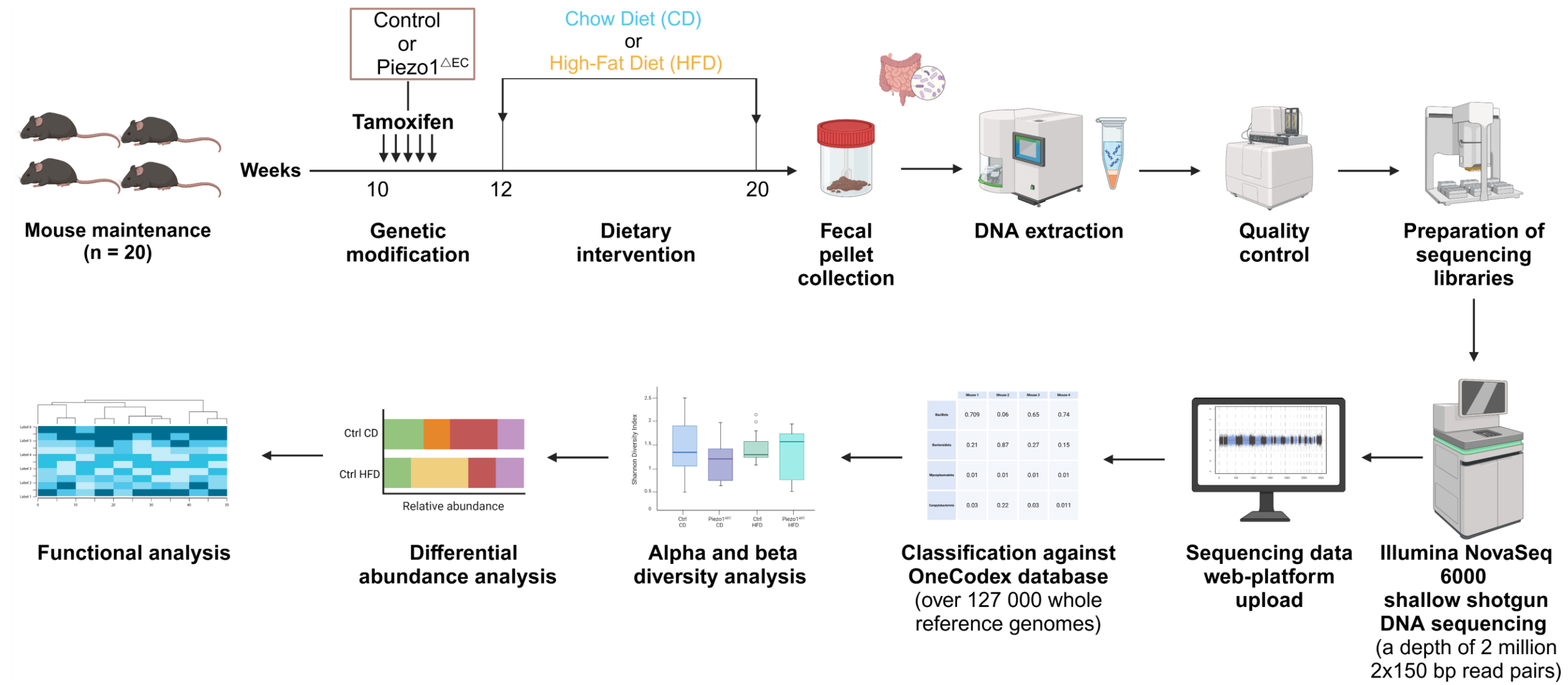
METHODS

Figure 2. Schematic workflow diagram. Created with Biorender.com (n=5 per group).

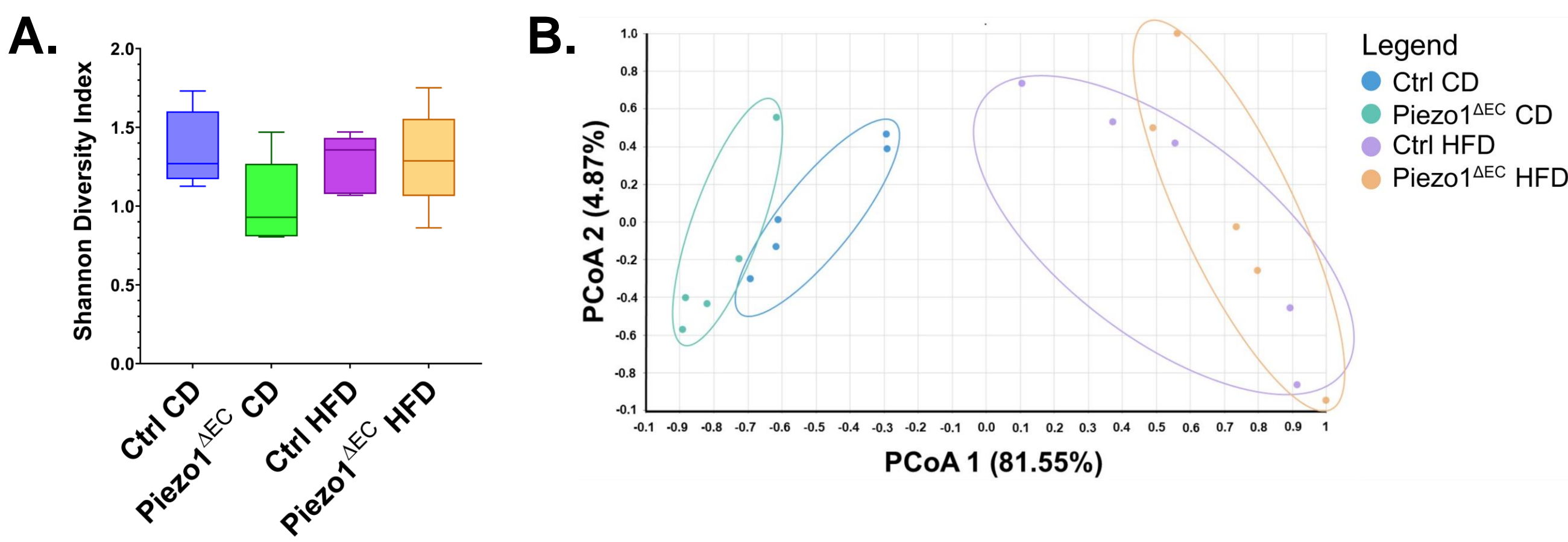## RESULTS: Alpha and Beta Diversity Analysis

Figure 3. Microbiome diversity analysis at phylum level across four study groups: control mice on chow diet (Ctrl CD), endothelial Piezo1 knockout mice on chow diet (Piezo1$^{\Delta EC}$ CD), control mice on high-fat diet (Ctrl HFD), and endothelial Piezo1 knockout mice on high-fat diet (Piezo1$^{\Delta EC}$ HFD). The analysis was conducted using OneCodex for microbiome data processing and R for statistical analysis. **A.** Alpha diversity analysis with Shannon index, visualised as a boxplot, showed no significant microbiome richness differences within individual groups, when compared across groups ($p>0.05$, Kruskal-Wallis test with Dunn's multiple comparisons test). The boxplot is shown as median (line), interquartile range (box), and minimum to maximum data range (whisker). **B.** Beta diversity analysis with weighted Unifrac Distance, visualised as a Principal Coordinates Analysis (PCoA) plot, demonstrated diet-based microbiome composition segregation between groups ($p<0.05$, PERMANOVA).

RESULTS: Taxonomic Composition and Differential Abundance Analysis
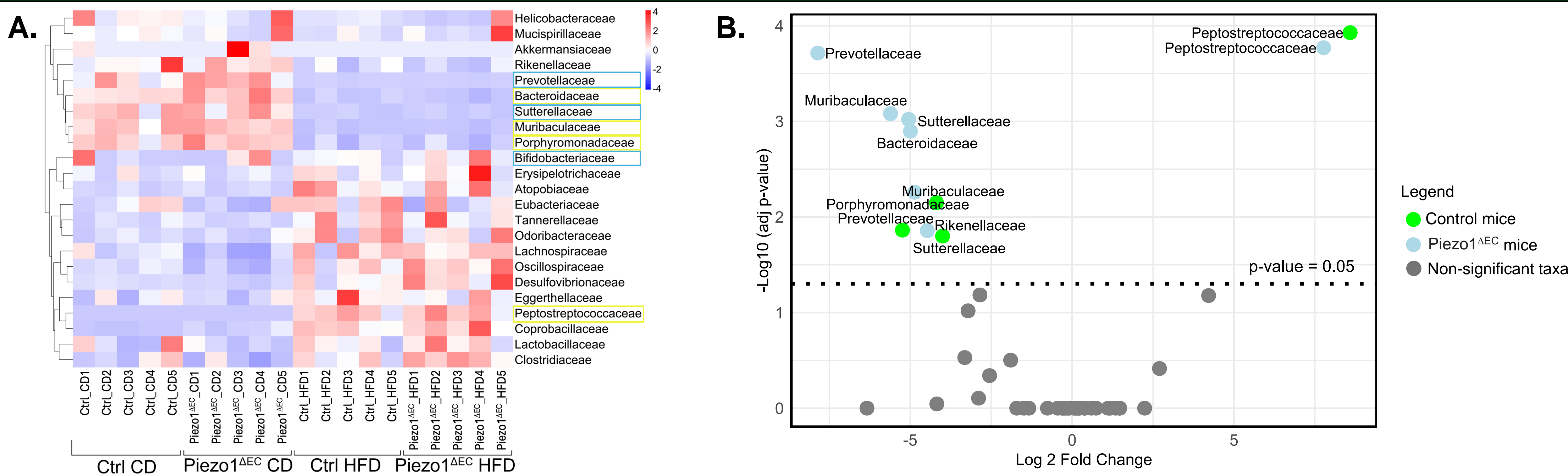

Figure 4. Family-level microbiome composition and differential abundance across four groups. The analysis was conducted using OneCodex for microbiome data processing and R for statistical analysis. Taxa present at > 1% were included. **A.** Hierarchical clustering of family-level taxa abundances in mice, calculated using Euclidean distance. Colour-coded boxes indicate differential abundance: yellow for taxa altered by high-fat diet in both control and Piezo1$^{\Delta EC}$ mice, and blue for taxa altered exclusively in Piezo1$^{\Delta EC}$ mice. **B.** The impact of a high-fat diet on family-level taxa abundance in Piezo1$^{\Delta EC}$ mice (blue) versus control mice (green), with grey dots indicating non-significant taxa. Differential abundance was analysed between Ctrl CD and Ctrl HFD for control mice, and between Piezo1$^{\Delta EC}$ CD and Piezo1$^{\Delta EC}$ HFD for Piezo1$^{\Delta EC}$ mice. Four families showed significant changes due to a high-fat diet in both control and Piezo1$^{\Delta EC}$ mice, with three additional families being differentially abundant exclusively in Piezo1$^{\Delta EC}$ mice ($p<0.05$, ANCOM-BC2).

CONCLUSIONS AND NEXT STEPS

- The analysis found no significant difference in microbiome richness within animal groups but significant microbiome segregation between groups due to high fat diet.
- In control and Piezo1$^{\Delta EC}$ mice, high-fat diet reduces beneficial, fibre-degrading bacteria such as Muribaculaceae and Prevotellaceae while increasing the abundance of Peptostreptococcaceae, which includes bacteria like Clostridioides difficile, indicating a shift towards pathogenic gut microbiome composition.
- **Next steps** include analysis of Piezo1 deletion effects on more granular taxonomic levels.