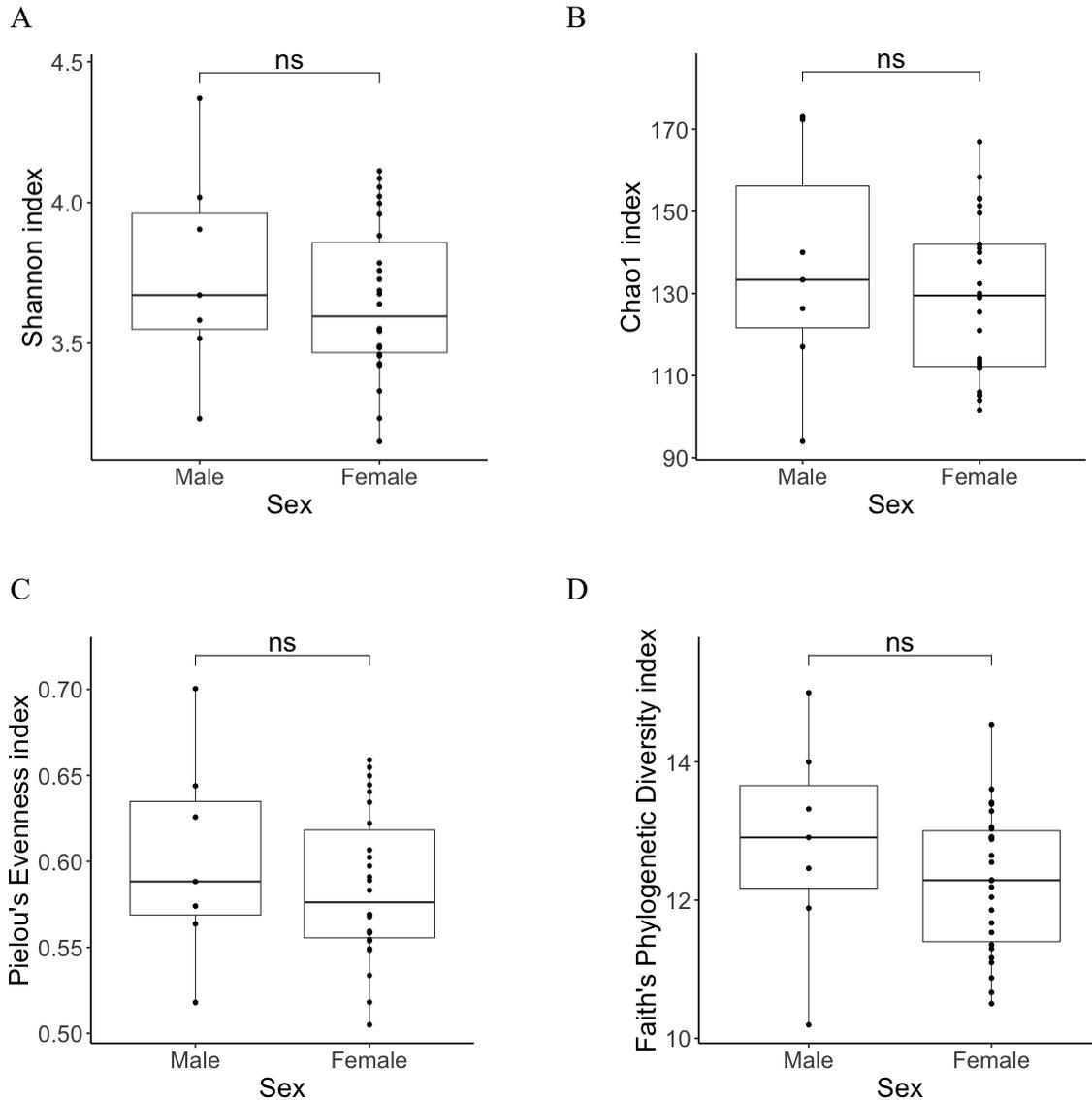
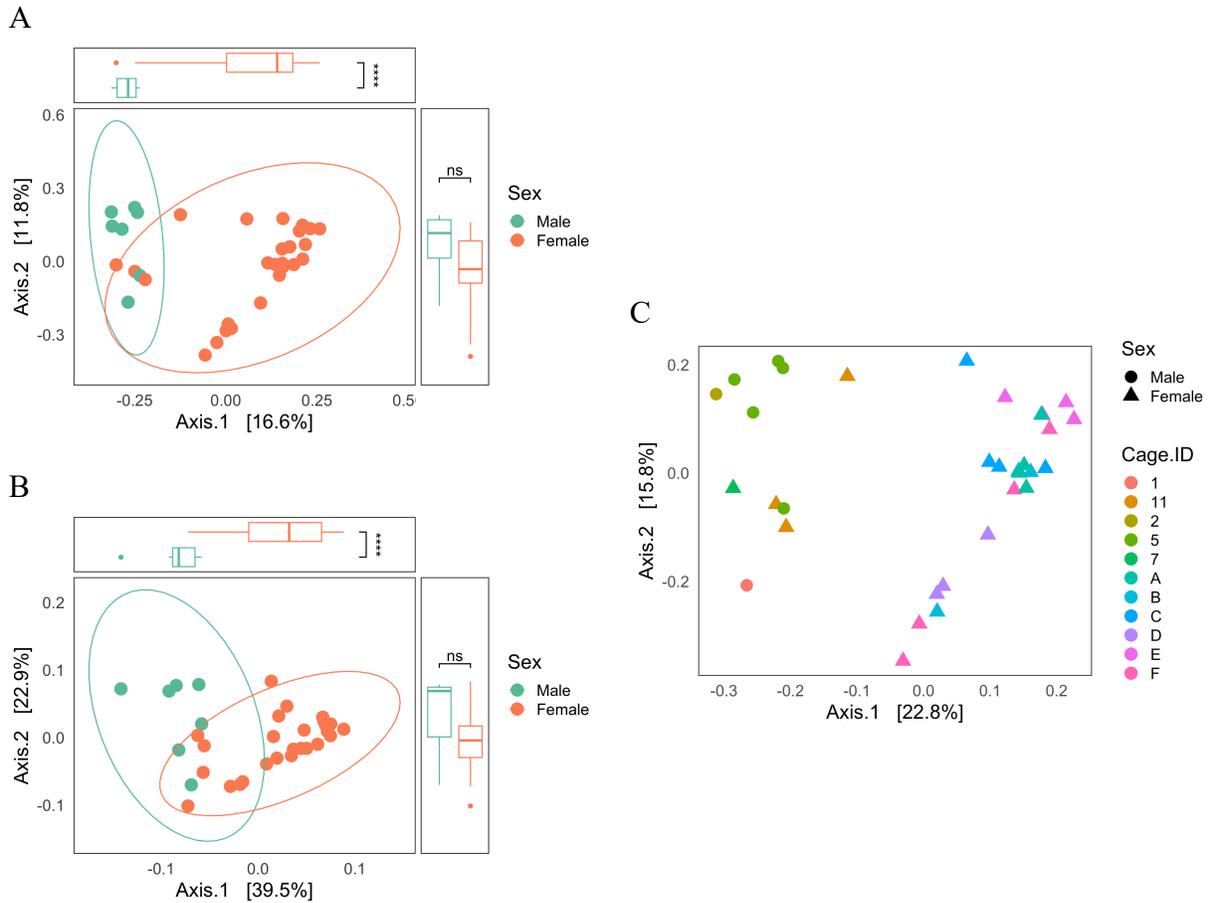


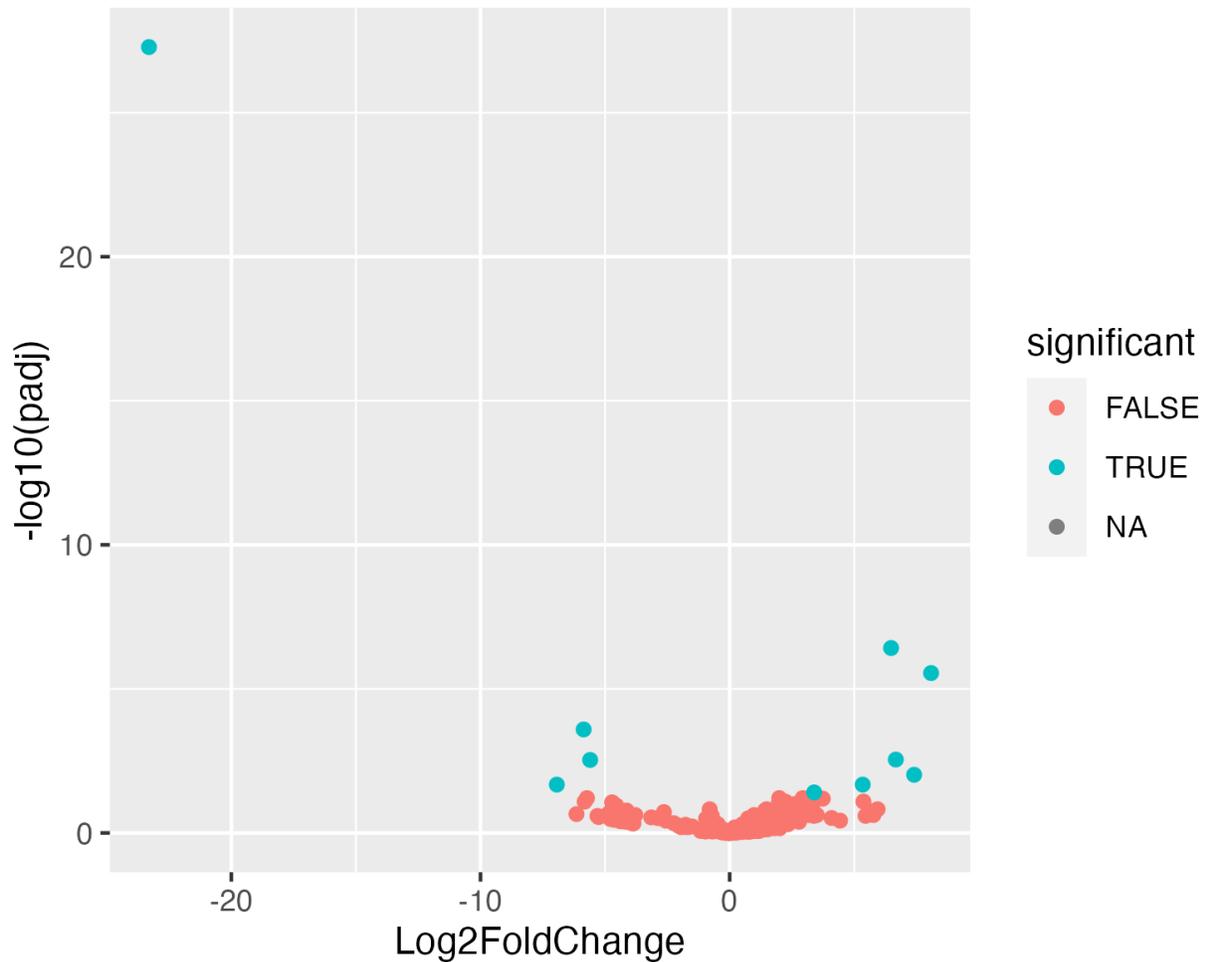
## SUPPLEMENTAL MATERIAL



**FIG. S1 Alpha diversity of mouse microbiome is similar between mouse sex.** Alpha diversity according to (A) Shannon Index, (B) Chao1 Index, (C) Pielou's evenness, and (D) Faith's phylogenetic diversity was compared between female and male. The data in the boxplots represent the 25th percentile, median, and 75th percentile; the whiskers stretch to 1.5 times the interquartile range (IQR) from the corresponding hinge. The comparison between sex for each alpha index was analyzed by Generalized Linear Model with age as a covariable following Gaussian distribution.  $n = 26$  for female and  $n = 7$  for male. ns: not significant;  $P > 0.05$ ;  $*P \leq 0.05$ ;  $**P \leq 0.01$ ;  $***P \leq 0.001$ ;  $****P \leq 0.0001$ .



**FIG. S2 Beta diversity of mouse microbiome is significantly different between sex.** PCoA illustrating the gut microbial compositions stratified by mouse sex based on (A) Jaccard (PERMANOVA,  $p = 0.11174$ ,  $R^2 = 0.001$ ) and (B) Weighted Unifrac (PERMANOVA,  $p = 0.001$ ,  $R^2 = 0.23416$ ) with a 95% ellipse for each group. The boxplots show the overall distribution of PCoA1 and PCoA2 scores for male and female. (C) Beta diversity of mouse microbiome representing by PCoA is similar across mice housed in different cages. The data in the boxplots represent the 25th percentile, median, and 75th percentile; the whiskers stretch to 1.5 times the interquartile range (IQR) from the corresponding hinge. An unpaired Wilcoxon rank-sum test was used.  $n = 26$  for female and  $n = 7$  for male. ns: not significant,  $p > 0.05$ ; \* $p \leq 0.05$ ; \*\* $p \leq 0.01$ ; \*\*\* $p \leq 0.001$ ; \*\*\*\* $p \leq 0.0001$ .



**FIG. S3 Male and female FD mice have multiple ASVs that are significantly different in abundance.** Volcano plot from differential expression sequence analysis showing different abundances of ASVs between female and male FD mice. The x-axis illustrates log2FoldChange and the y-axis illustrates negative log10 adjusted p-value. Reference group was set to be female FD mice. Blue plots represent significantly differentially abundant taxa ( $p\text{-adjusted} < 0.05$  and  $\log_2\text{FoldChange} > 1.5$ ), while red plots represent taxa non-significantly differentially abundant in males.  $n = 21$  for female and  $n = 13$  for male.