

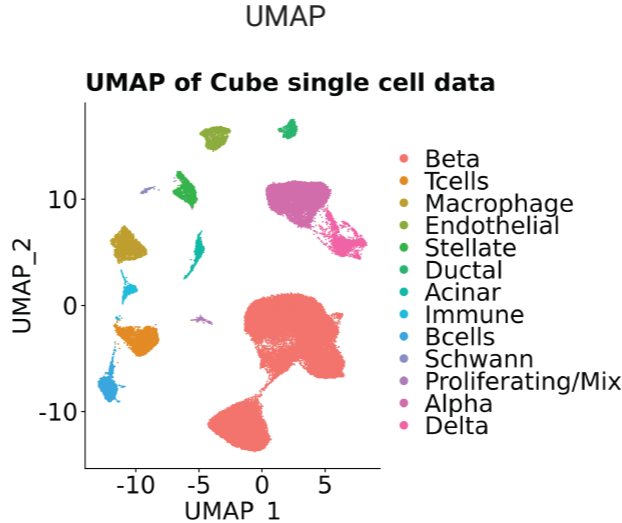
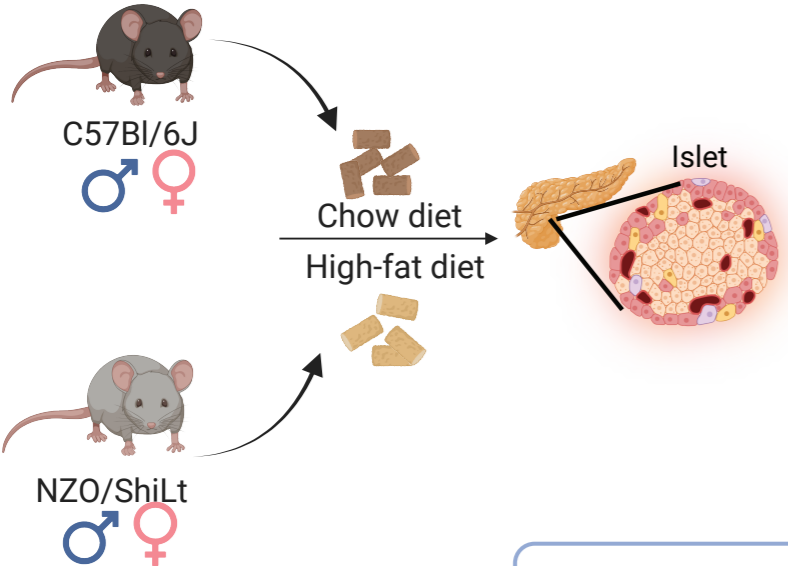
600 **Figure S0: Workflow of meta-cell ssNPA (single-cell Network Perturbation Analysis) using data**
601 **from mice fed with either a high-fat or chow diet.** This schematic outlines the process of analyzing
602 cell-specific gene expression and perturbation scores.

603 **Figure S0': This is an example of an Abcc8 perturbation case where DEG (Differentially**
604 **Expressed Gene) analysis fails to detect significant changes.** It showcases the specificity and
605 sensitivity of ssNPA.

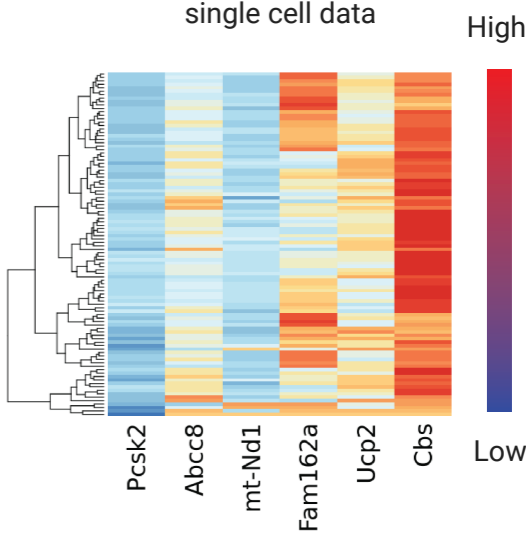
606 **Figure S1: Full network analysis from β -cells of C57BL/6J mice fed on a regular or high-fat,**
607 **high-sugar diet, displaying the network's complex interactions and expression levels.**

608 **Figure S2: t-SNE plots illustrating perturbation scores comparing NZO and C57BL/6J male mice**
609 **on high-fat diets, highlighting differences in gene expression profiles between the strains.**

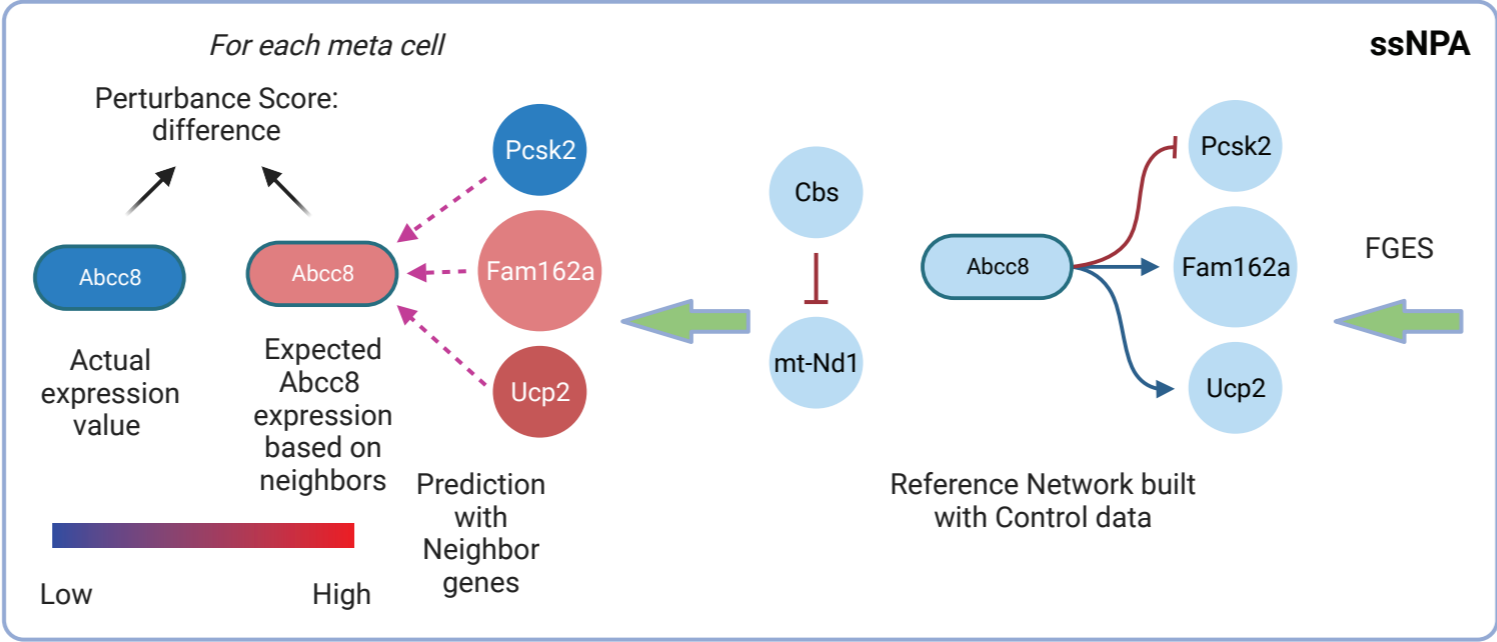
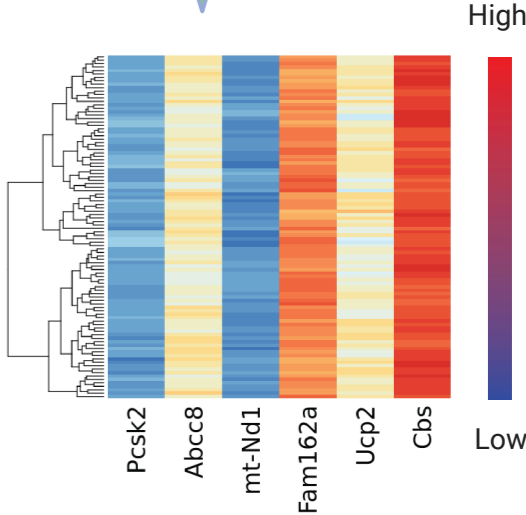
Figure S0: Workflow of meta-cell ssNPA analysis



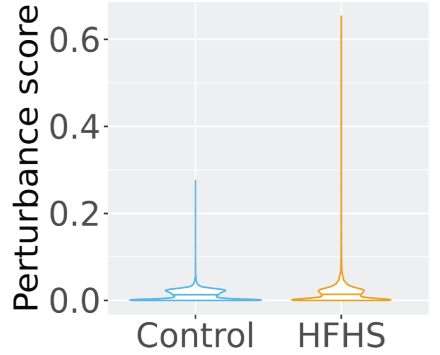
For one selected strain and cell types



meta-cell samples

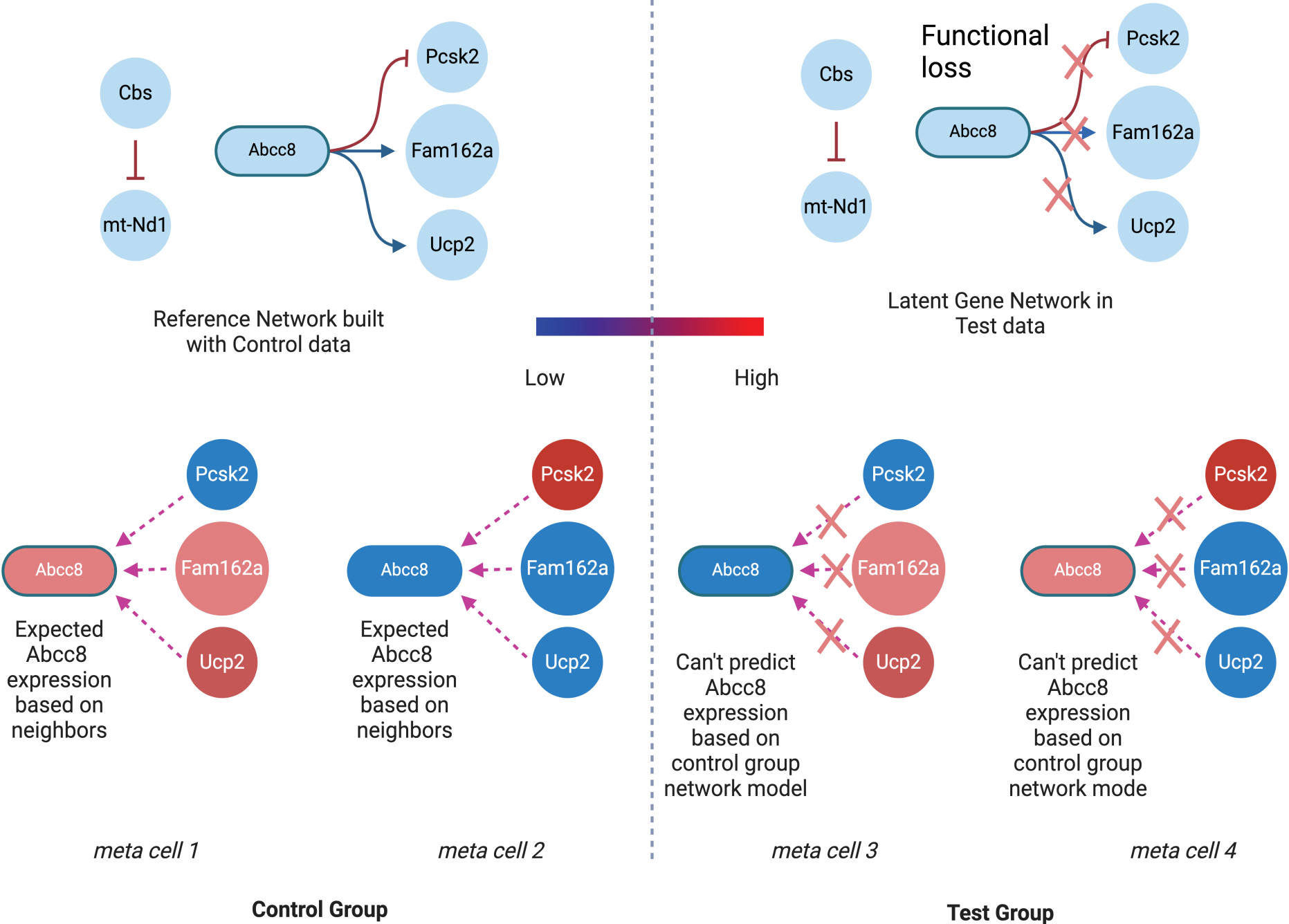


Abcc8 is a Perturbed Gene: Wilcoxon test FDR < 0.05



Control Perturbance Score: will be low since the network is trained with control group data

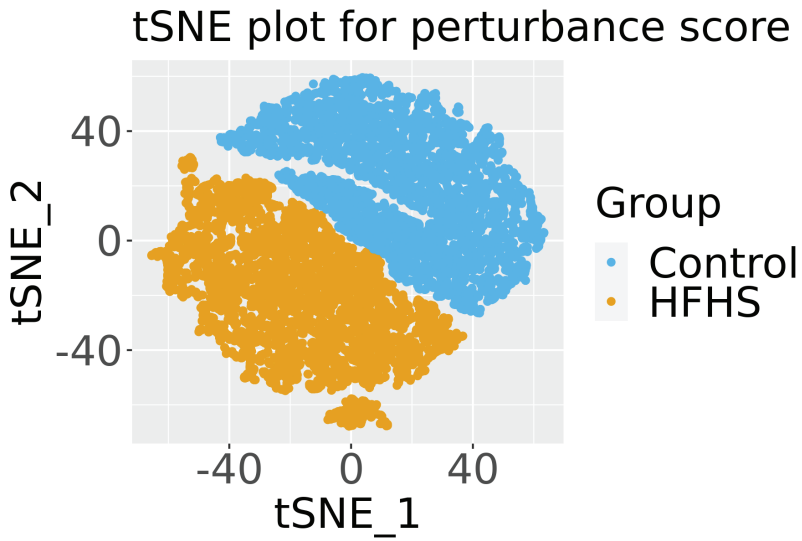
Figure S0': An example Abcc8 perturbation case where DEG analysis can't detect



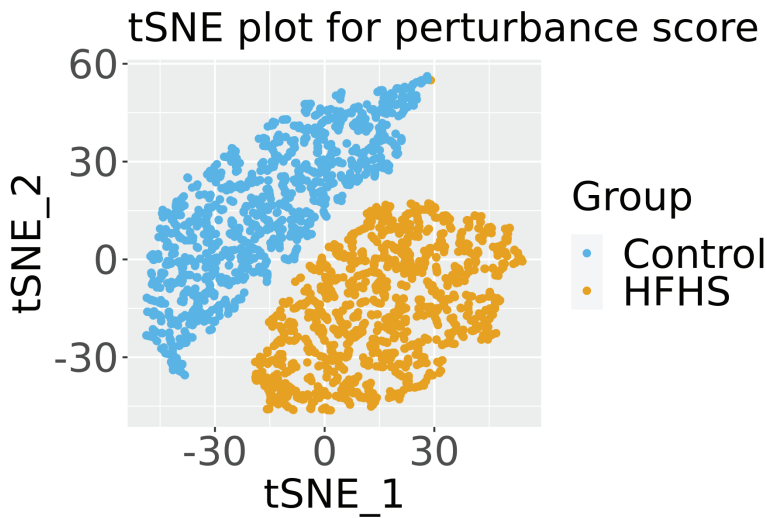
DEG analysis on Abcc8 between meta cell 1, meta cell 2 and meta cell 3, meta cell 4 will have p-value > 0.05

Figure S2: t-sne plots for petrubance score

B6 Male



NZO Male



NZO HF vs B6 HF Male

