

Description of Additional Supplementary Files

Title: **Supplementary Data 1**

Description:

Sheet 1:

Differentially expressed genes comparing hepatocytes from the double mutant and control mice

Sheet 2:

Differentially expressed genes comparing LSEC from the double mutant and control mice

Pseudobulk samples were extracted from scRNA-seq data and DEGs between genotypes were calculated using DESeq2. Details can be found in "Single-cell RNA-seq analysis" of the method.

Title: **Supplementary Data 2**

Description:

Sheet 1:

Differentially expressed genes comparing hepatocytes from the double mutant and control mice across different zones

Sheet 2:

Differentially expressed genes comparing LSEC from the double mutant and control mice across different zones

Zonation coordinates are assigned as (0,2=central, 0,5=midzonal, 0,8=portal).

Wald testing was used for statistical analysis. Details can be found in "Assignment of zonation position", "Smoothing gene expression along zonation", and "Ranked position score" of the method.

Title: **Supplementary Data 3**

Description:

Sheet 1:

Log2-transformed LFQ intensity of hepatocytes from the double mutant and control mice

Sheet 2:

Log2-transformed LFQ intensity of LSEC from the double mutant and control mice

Details can be found in "Analysis of raw MS data" of the method.

Title: **Supplementary Data 4**

Description:

Sheet 1:

Metabolite Reporting Checklist

Sheet 2:

Mass Spectrometry-guided metabolite screening of blood plasma and whole liver lysates from the double mutant and control mice