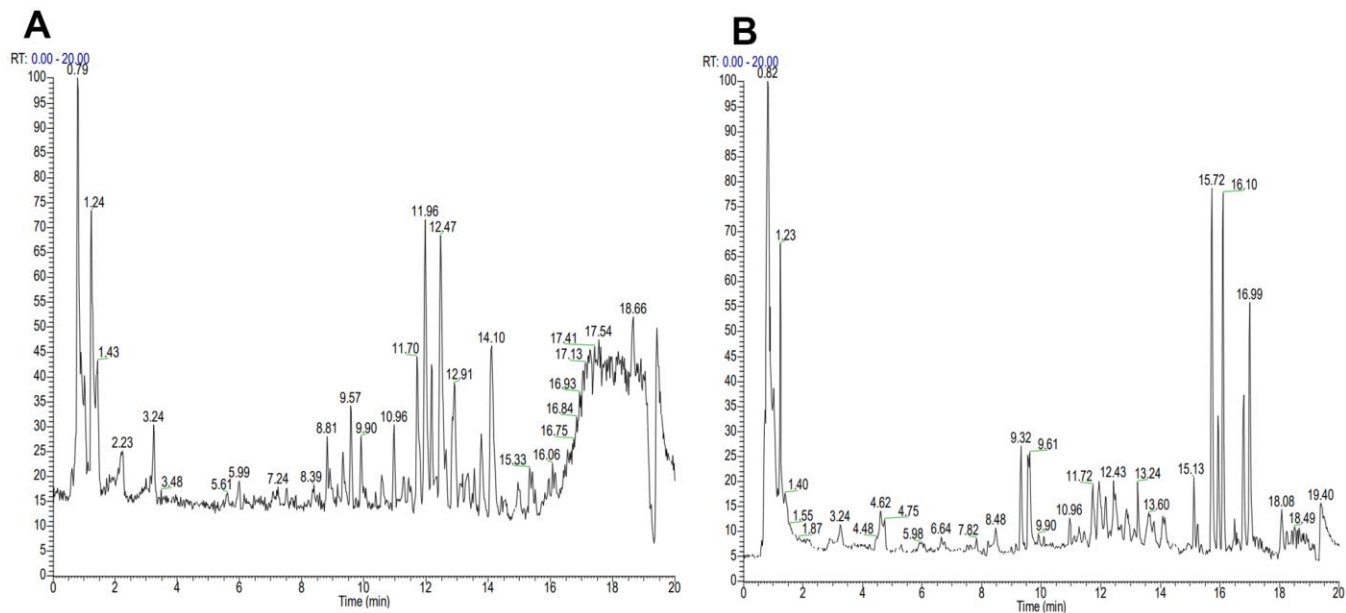
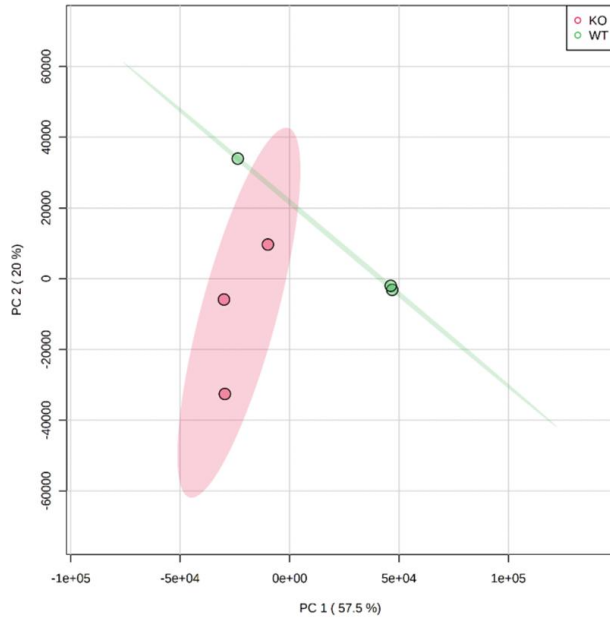
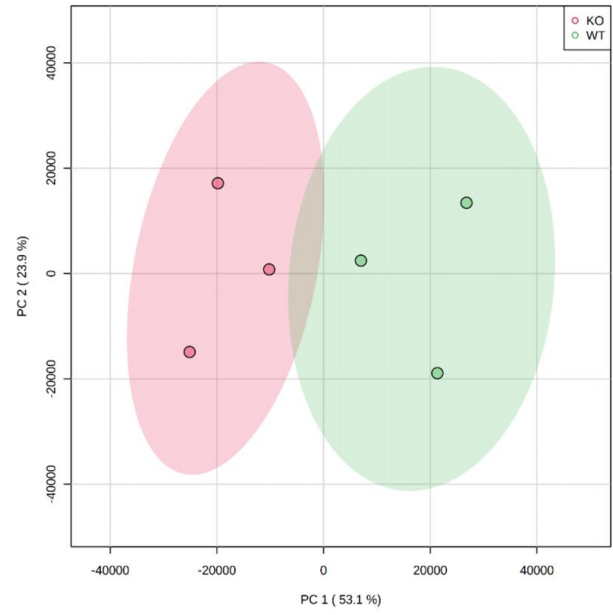
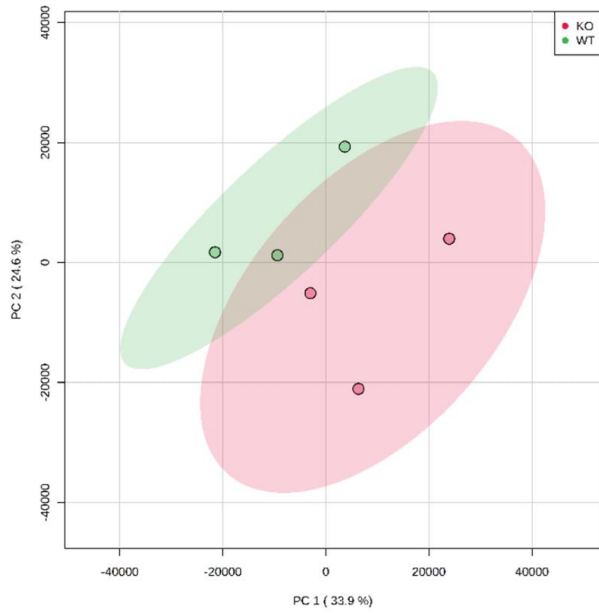
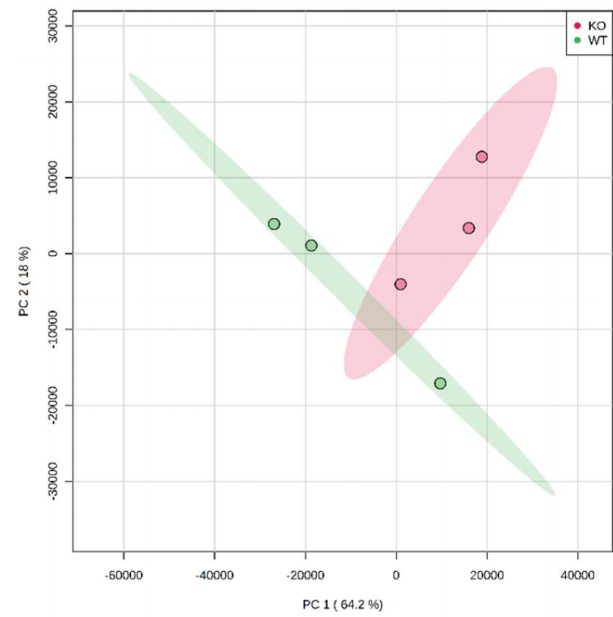


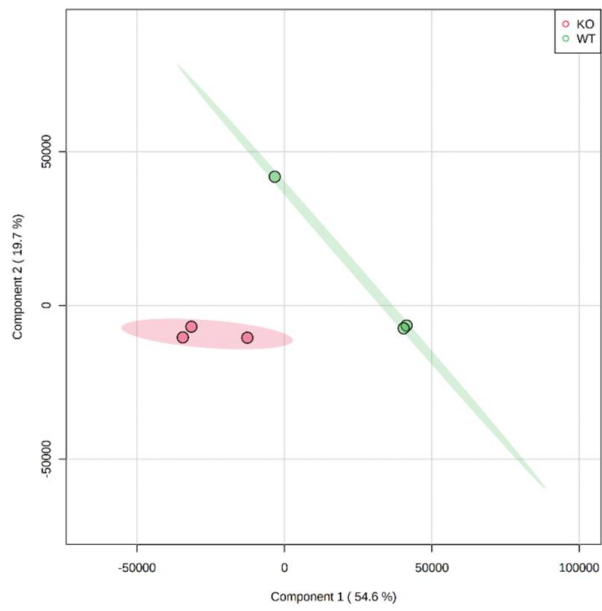
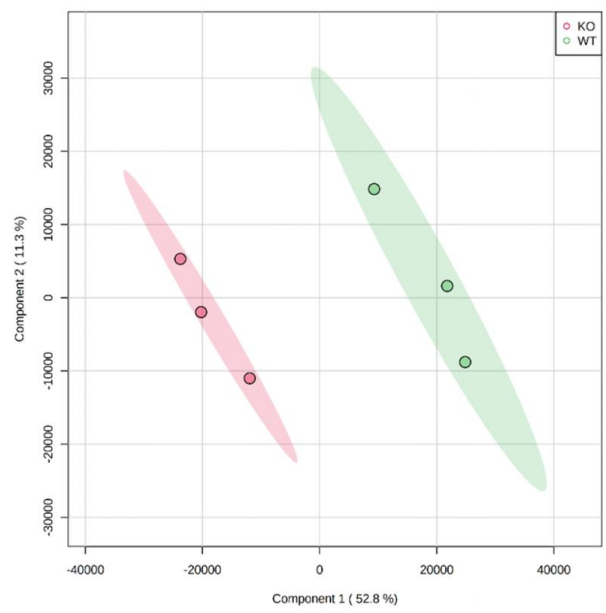
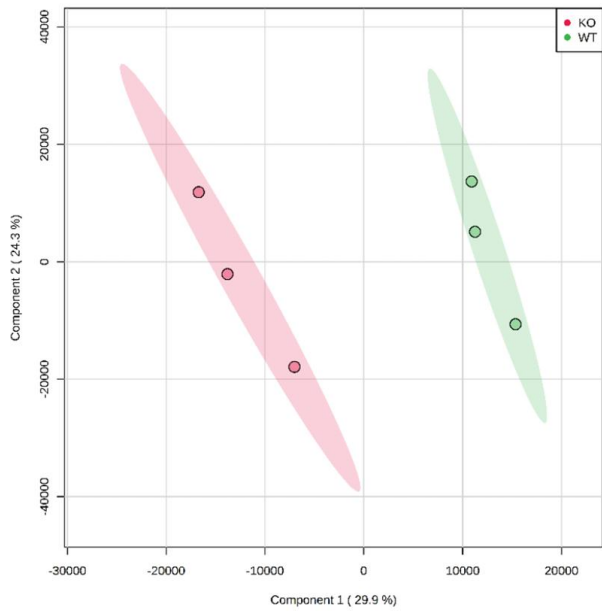
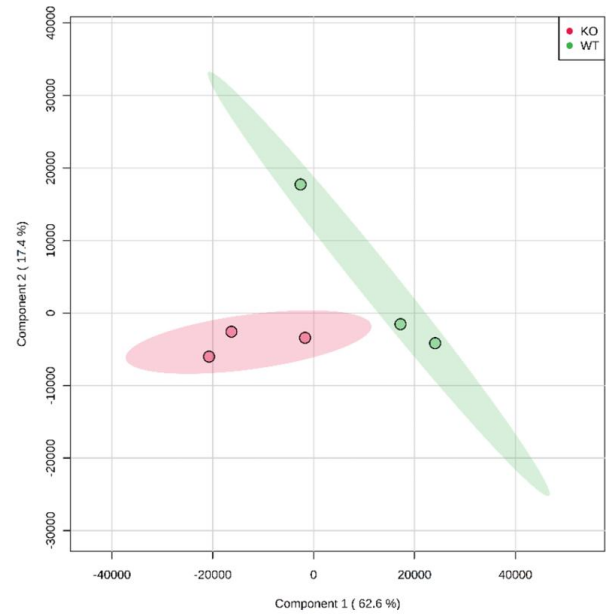
SUPPLEMENTARY FIGURES



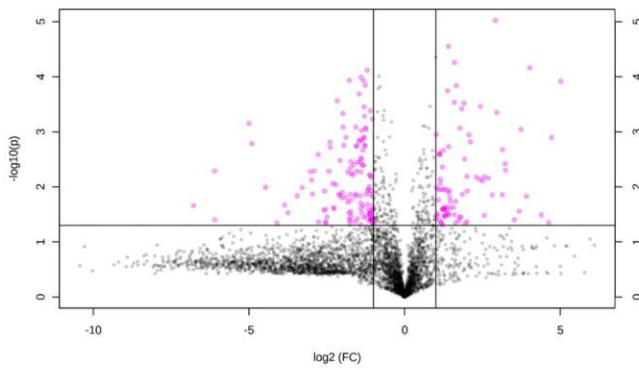
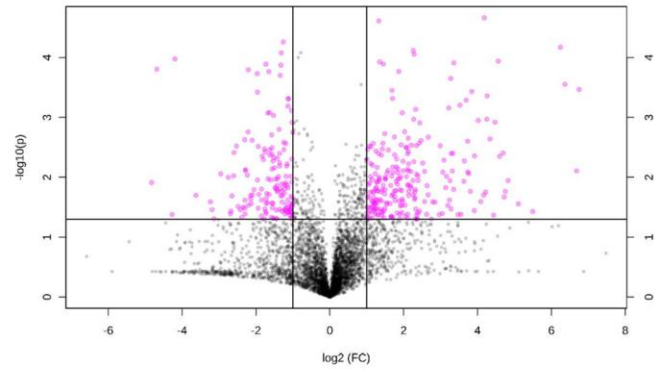
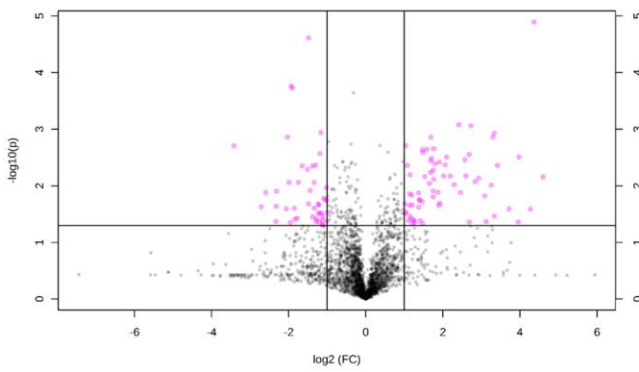
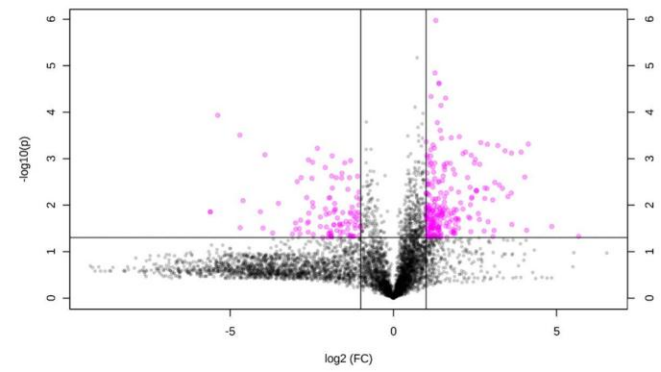
Supplementary Figure 1. Base peak intensity (BPI) chromatograms obtained from mouse plasma in liquid chromatography mass spectrometry (LC-MS). (A) Positive (ESI⁺) scan mode, (B) negative (ESI⁻) scan mode.

A**B****C****D**

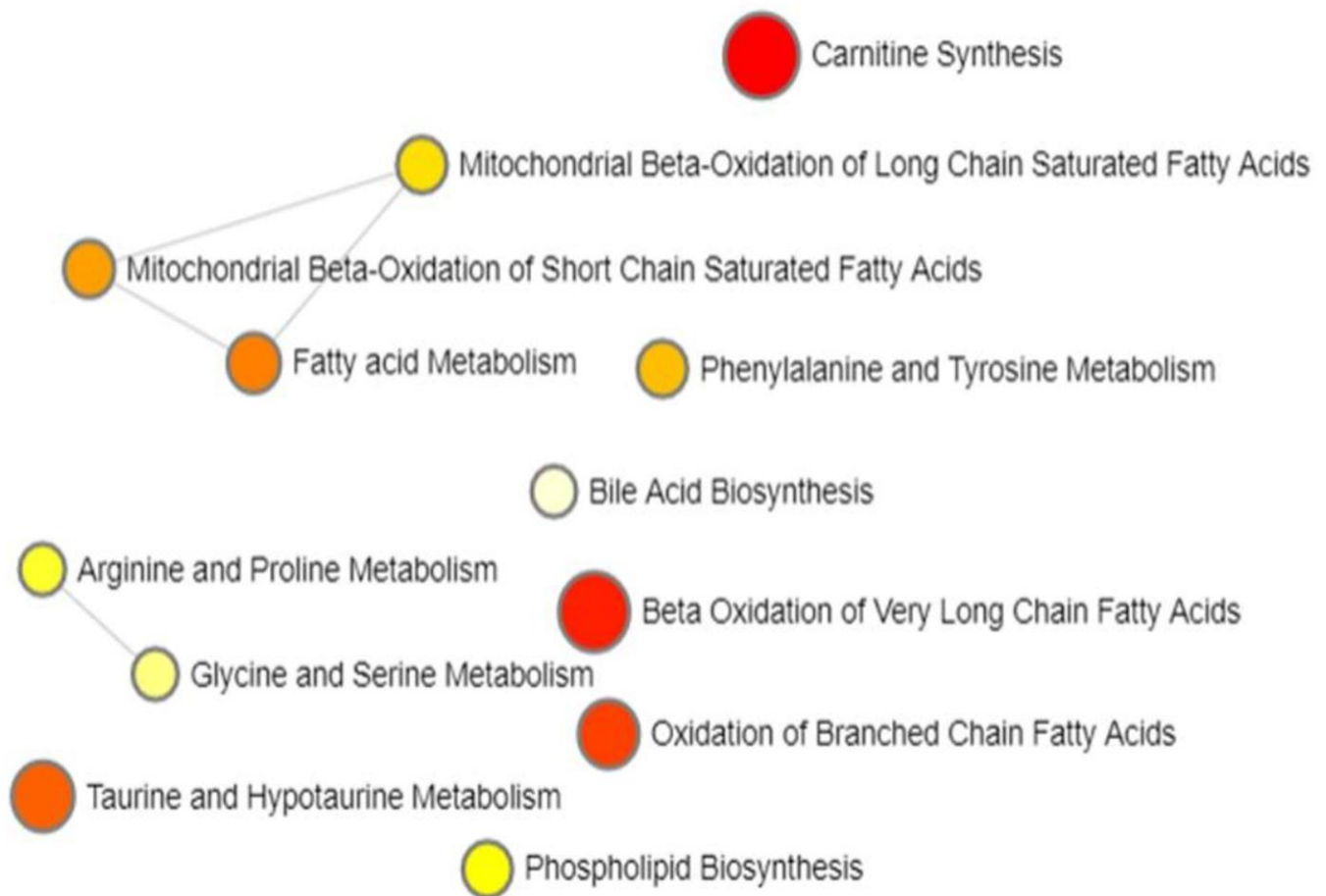
Supplementary Figure 2. Score scatter plot of PCA model. (A) $ES1^+$ scan in 50-week-old mice; (B) $ES1^-$ scan in 50-week-old mice; (C) $ES1^+$ scan in 100-week-old mice; (D) $ES1^-$ scan in 100-week-old mice. Magenta circles indicate MTKO mice and green circles indicate WT mice.

A**B****C****D**

Supplementary Figure 3. Score scatter plot of PLS-DA model. (A) ESI^+ scan in 50-week-old mice; (B) ESI^- scan in 50-week-old mice; (C) ESI^+ scan in 100-week-old mice; (D) ESI^- scan in 100-week-old mice. Magenta circles indicate MTKO mice and green circles indicate WT mice.

A**B****C****D**

Supplementary Figure 4. Volcano plot of data. The ranges, $Y > 1.30$ and $X > 1$, indicate a significant increase; the ranges, $Y > 1.30$ and $X < -1$, indicate a significant decrease (magenta circles). **(A)** ESI⁺ scan in 50-week-old mice; **(B)** ESI⁻ scan in 50-week-old mice; **(C)** ESI⁺ scan in 100-week-old mice; **(D)** ESI⁻ scan in 100-week-old mice.



Supplementary Figure 5. A correlation network diagram obtained from pathway enrichment analysis of perturbed metabolites in 100-week old MTKO mice in ESI⁺ mode. Each node denotes one different function, while more significant functions are indicated by a darker color.