

**Figure S1. Genotyping products of SIRT2-WT and SIRT2-KO rats.** Product sizes were 540 and 380 bp for WT and KO alleles, respectively.

**Figure S2. Metabolic phenotype in female SIRT2-WT and SIRT2-KO rats.** (A) Body weight curves of SIRT2-WT and SIRT2-KO rats ( $n=6$ ). (B) Food intake in SIRT2-WT and SIRT2-KO rats at ~15 weeks of age ( $n=4$ ). (C) Random blood glucose ( $n=15$ ). (D) Blood glucose levels in body weight-matched rats were measured at the indicated times after 16-h fasting during IPGTT( $n=14$ ). Data are expressed as means  $\pm$  SEM. \*\* $P < 0.01$ , \*\*\* $P < 0.001$  vs WT rats.

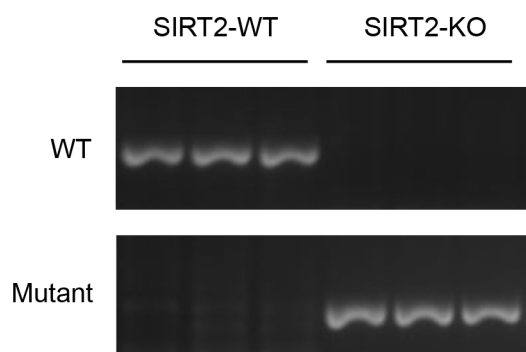
**Figure S3. SIRT2 knockout or inhibition has no impact on gluconeogenic gene expressions.** (A-B) mRNA and protein expressions of PEPCK in the liver of SIRT2-WT and SIRT2-KO male rats under the status of fasting or refeeding ( $n=4$ ). (C) mRNA expression of gluconeogenic genes in the liver of SIRT2-WT and SIRT2-KO male rats ( $n=4$ ). (D) Protein level of PEPCK in primary mouse hepatocytes treated with 3  $\mu$ M AGK2. Data are expressed as means  $\pm$  SEM. \*\*\* $P < 0.001$  vs WT rats.

**Figure S4. mRNA level of SIRT2 in rat islets at low and high glucose concentrations.**

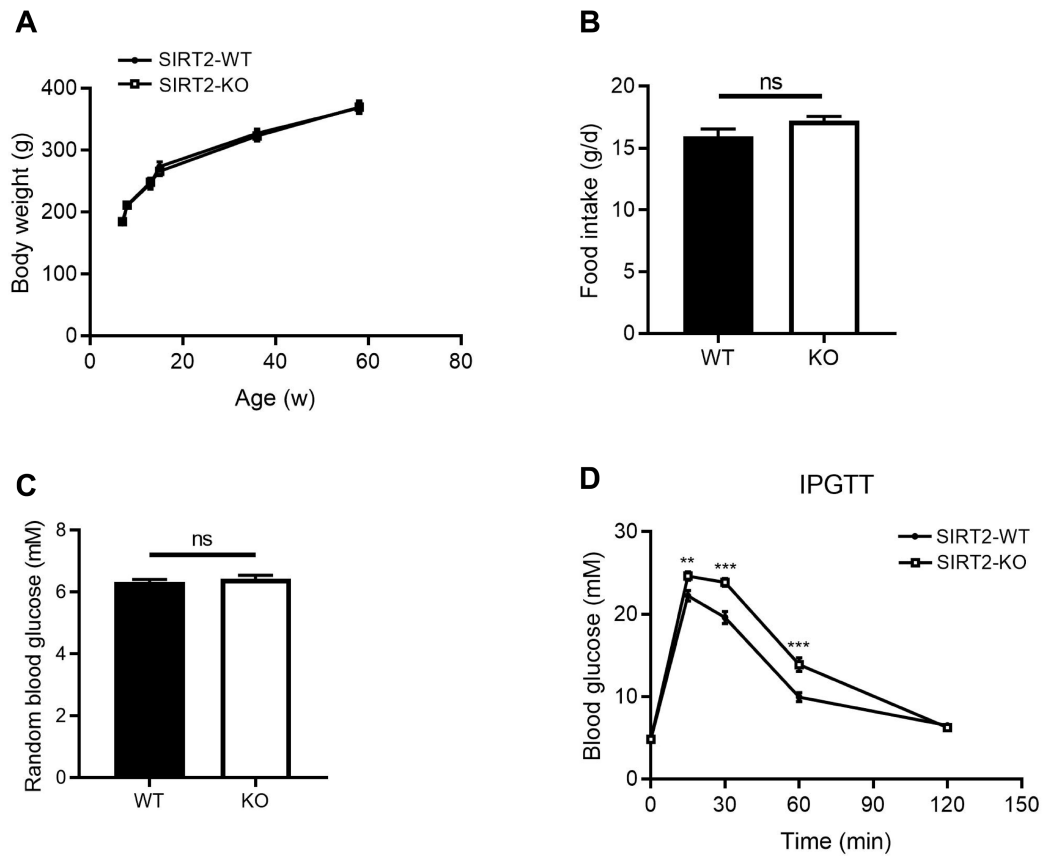
**Figure S5. Visualization of metabolite profiles is presented by volcano-plots.** Up-regulated and down-regulated metabolites in SIRT2-KO islets versus SIRT2-WT islets were distributed in the right and left side, respectively (VIP > 1, blue points indicate  $P < 0.1$ , green points indicate  $P < 0.05$ ).

**Figure S6. mRNA expressions of three aldolase isozymes (A, B, and C) in rat islets.** Data are expressed as means  $\pm$  SEM. \*\*\* $P < 0.001$  vs ALDOA.

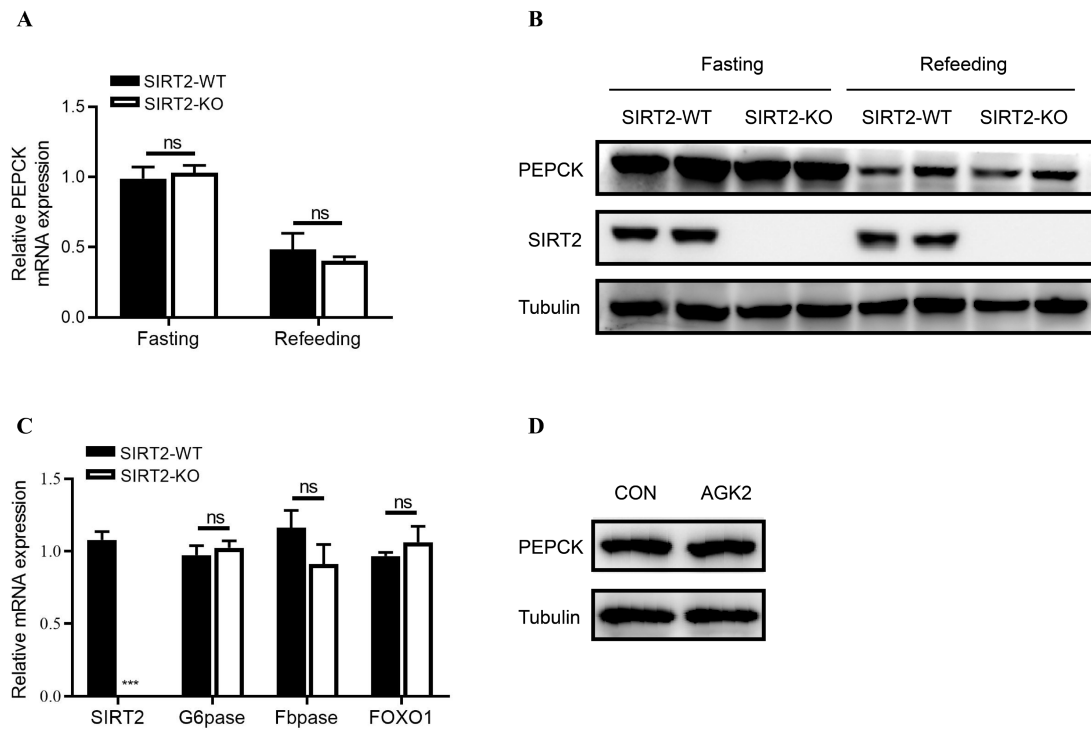
**Figure S1**



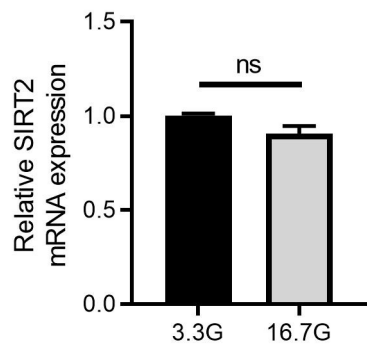
**Figure S2**



**Figure S3**



**Figure S4**





**Figure S6**

