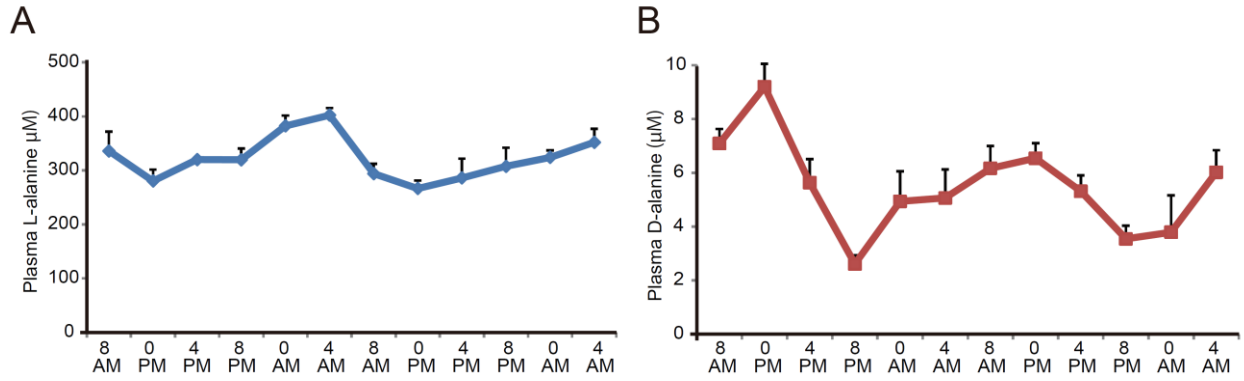


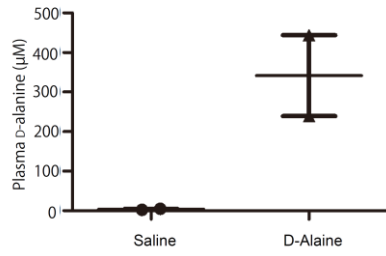
## **Supplementary Materials**

**D-Alanine affects the circadian clock to regulate glucose metabolism in kidney**

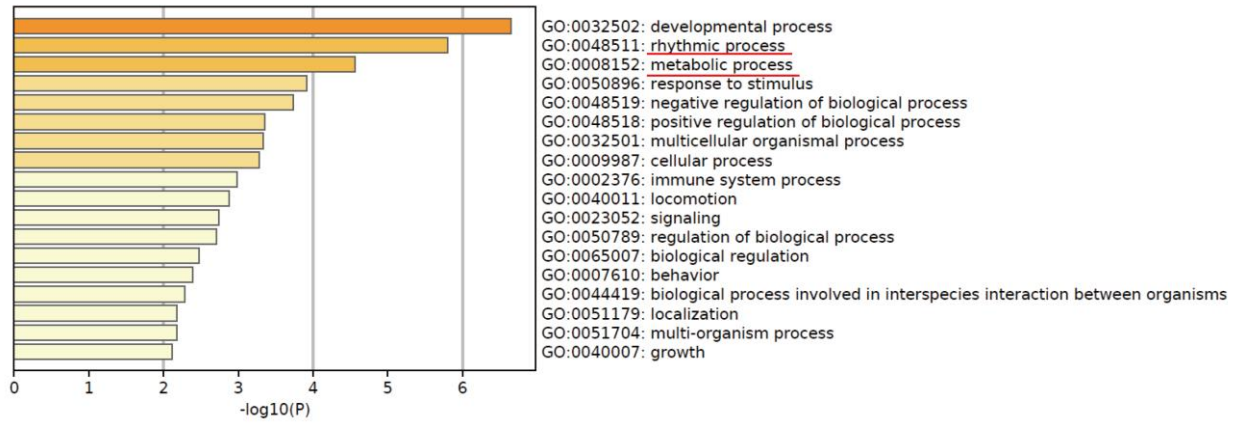
4 Supplementary figures



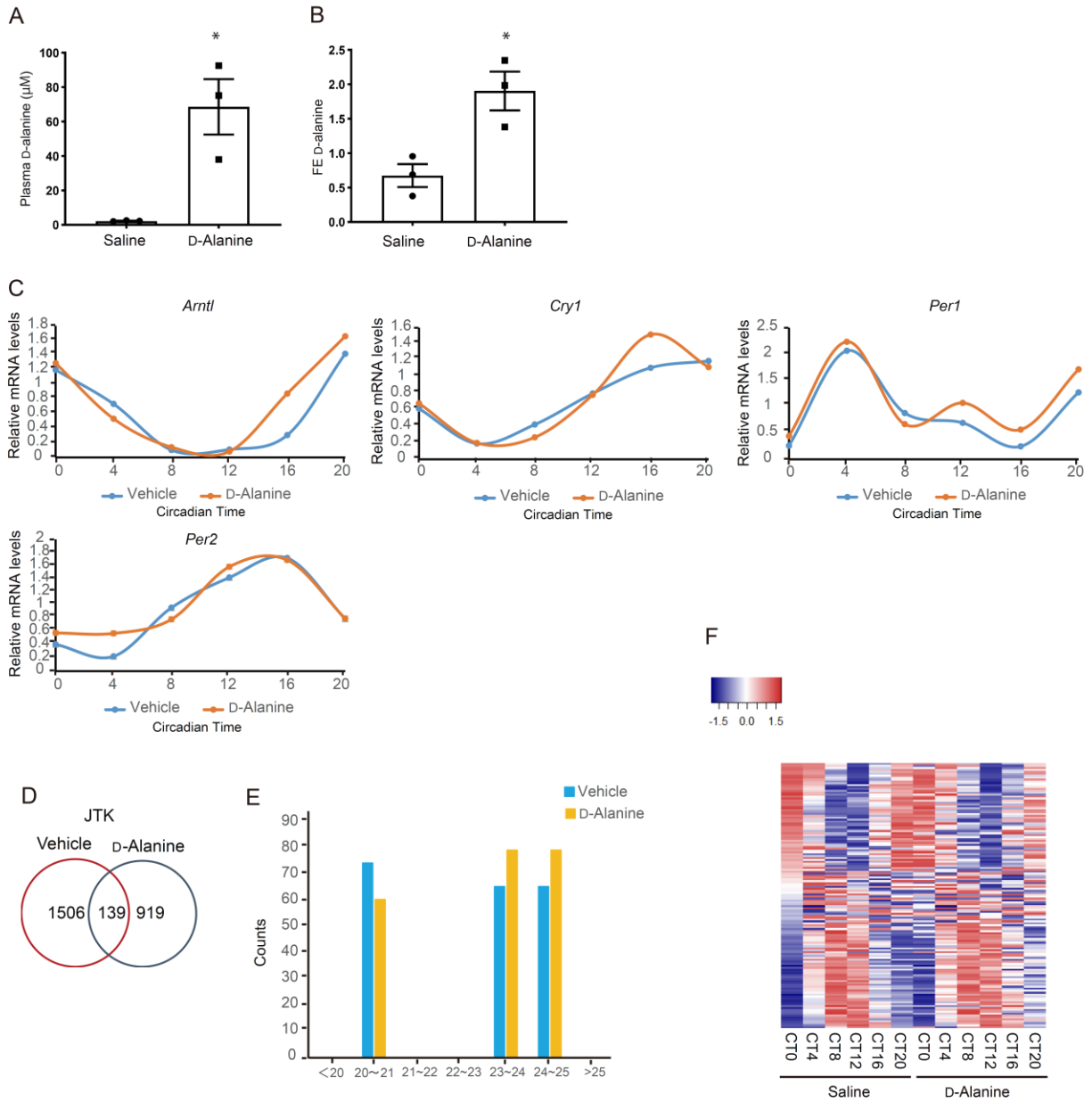
**Supplementary Figure S1. D-Alanine has an intrinsic circadian rhythm.** (A) Plasma L- and D-alanine levels of mice bred under a 12-h light: 12-h dark (LD) cycle condition (L, 8 AM–8 PM; D, 8 PM–8 AM).  $n = 4$ .



**Supplementary Figure S2. Plasma level of D-alanine in mice.** Mice were intraperitoneally treated with 12.5  $\mu\text{mol/g}$  of D-alanine for three times with 12-h of interval. Blood samples were harvested 2 h after last injection.  $n = 2$ .



**Supplementary Figure S3. D-Alanine modifies transcripts of circadian and gluconeogenic genes in kidney.** Gene ontology analysis of kidney from mice that received intraperitoneally treated with vehicle or D-alanine. Kidneys were harvested 2 h after treatment.



**Supplementary Figure S4. D- Alanine normalizes circadian cycles in constant darkness.** (A and B) (A) Plasma level and (B) fractional excretion (FE) of D-alanine in mice that were orally treated with either saline or D-alanine under constant darkness conditions. (C) Expression level of rhythmic genes at each time point in the kidney from saline or D-alanine treated-mice. (D) Venn diagram representing rhythmic genes of the kidney from saline or D-alanine-treated mice. Rhythmic genes were identified using JTK.  $n=4$ . (E) Number of common rhythmic genes identified using JTK algorithm in kidney from vehicle- and D-alanine-treated mice. (F) Heatmap of common rhythmic genes identified using JTK in kidney from vehicle- and D-alanine-treated mice. CT, circadian time. Data, means  $\pm$  SE. Statistic, two-tailed unpaired  $t$ -test. \* $P < 0.05$ .