

Supplementary Information

Supplementary Figure legends

Fig. S1. LLDT-8 induced spermatocyte-specific testis toxicity in C57BL/6 mice. (A) body weight. (B) Testis weight. (C) Epididymis weight of mice. (D) Testis morphology of 'Saline' group. (E-G) The transcript levels of germ cell-specific differentiation markers (Gata1, Plzf, and Prm1) in the testes were detected by qRT-PCR. Gata1: a marker for sertoli cells; Plzf: a marker for germ stem cells and type A spermatogonia; Prm1: a marker for spermatids. Significant difference was determined by one way Anova, n=3-5, mean \pm SD. ** P<0.01, *** P<0.001.

Fig. S2. LLDT-8 did not induce any abnormality in other tissues including liver, kidney and circulation. Serum levels of alanine aminotransferase (ALT), aspartate transaminase (AST), blood urea nitrogen (BUN), creatine (Cre), creatine Kinase (CK), alkaline phosphatase (ALP) were shown in Fig. S3A-F. Routine blood test results of white blood cell (WBC), neutrophil (NEUT), lymphocyte (LYM), monocyte (MONO), red blood cell (RBC), blood platelet (PLT) were shown in Fig. S3G-L.

Fig. S3. LLDT-8 did not induce any abnormality in liver, kidney, spleen and epididymis in C57BL/6 mice. (A) Liver morphology of mice. CV: central venous. (B) Kidney morphology. *: glomerular. (C) Spleen morphology. *: arteriole. (D) Caput epididymis morphology. (E) Cauda epididymis morphology.

Fig. S4. The distribution of γ -H2AX in the testes after LLDT-8 administration.

Fig. S5. LLDT-8 affected the expression of several MAPKs. After incubated with LLDT-8 for 16h, the expression of multiple MAPKs in GC-2spd lysates was detected by western blotting.

Fig. S6. The effects of LLDT-8 on the transcription level of Tak1 in GC-2spd cells. After treatment with LLDT-8 (250, 500nM) for 8h, 16h, and 24h, the transcript levels of TAK1 of GC-2spd were

detected by qRT-PCR. The data were shown as mean \pm SD. Significant difference was determined by one way Anova, $n = 3$, *** $P < 0.001$ vs control.

Fig. S7. The expression of RNA polymerase II was downregulated by LLDT-8 in GC-2spd. Cells were incubated in various doses of LLDT-8 for 16h.

Fig. S8. Representative results. (A) Representative results in Fig. 3B. (B) Representative results in Fig. 5D. (C) and (D) Representative results in Fig. 6F. (E) and (F) Representative results in Fig. 7C. Cellular apoptosis was analyzed by flow cytometry.

Fig. S1. LLDT-8 induced spermatocyte-specific testis toxicity in C57BL/6 mice.

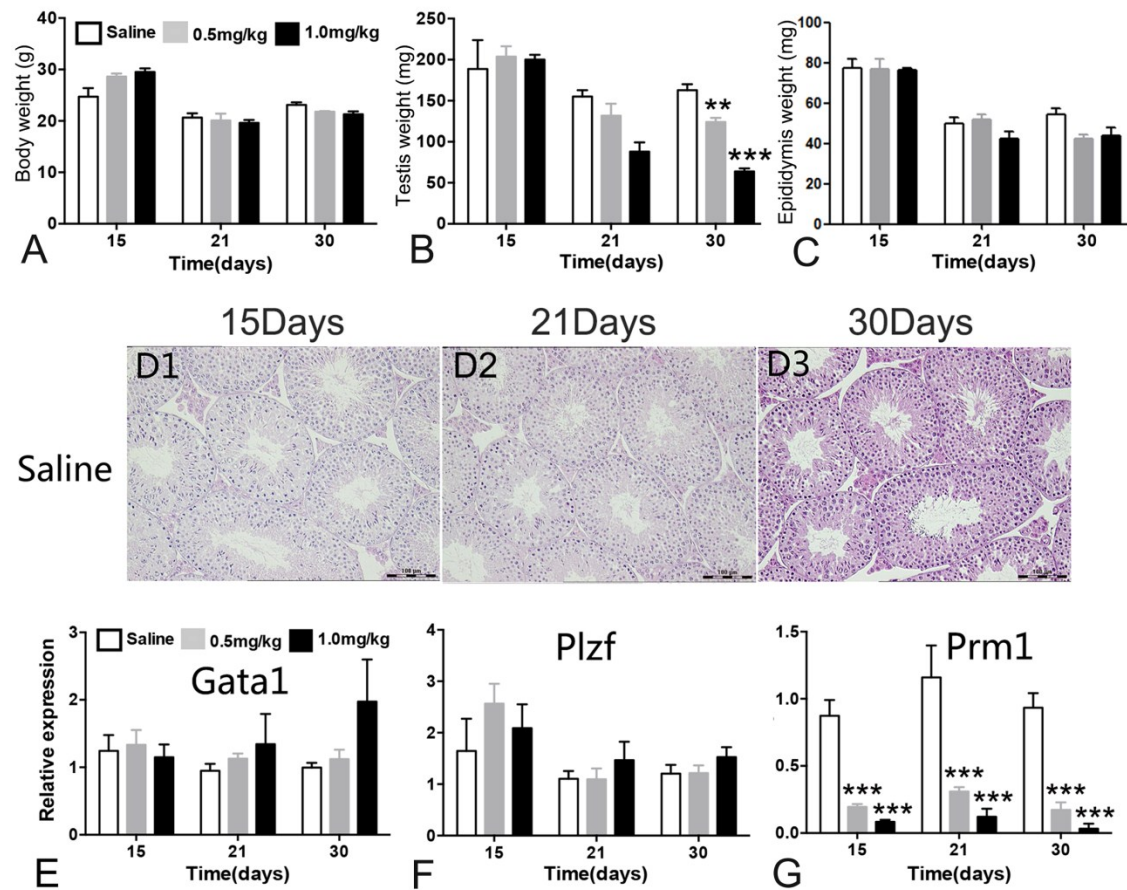


Fig. S2. LLDT-8 did not induce any abnormality in other tissues including liver, kidney and circulation.

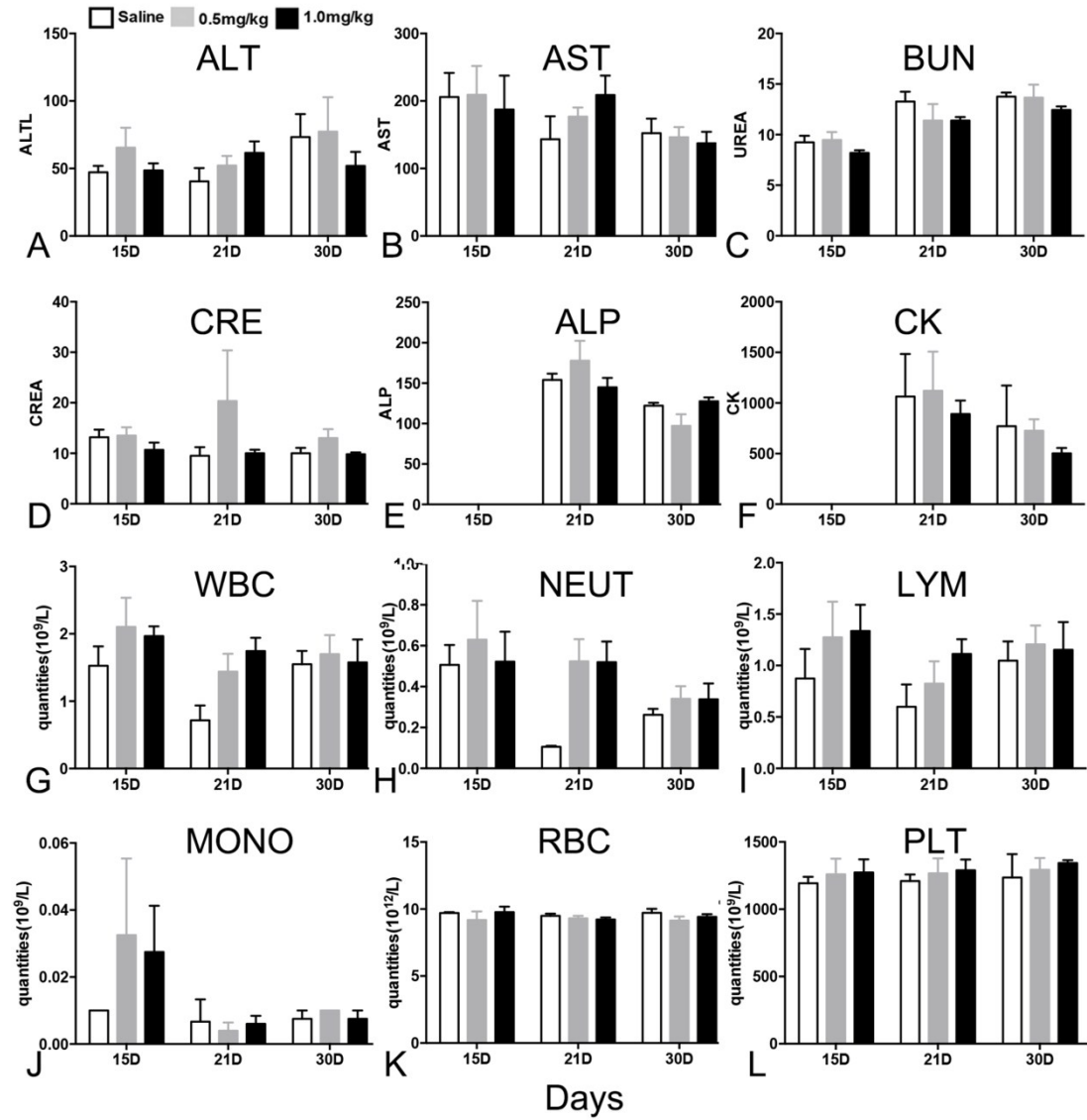


Fig. S3. LLDT-8 did not induce any abnormality in liver, kidney, spleen and epididymis in C57BL/6 mice.

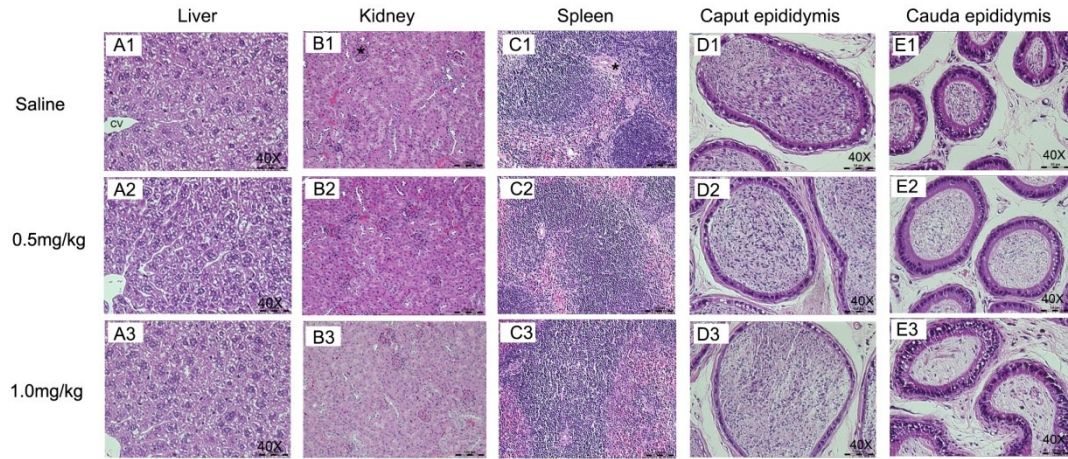


Fig. S4. The distribution of γ -H2AX in the testes after LLDT-8 administration.

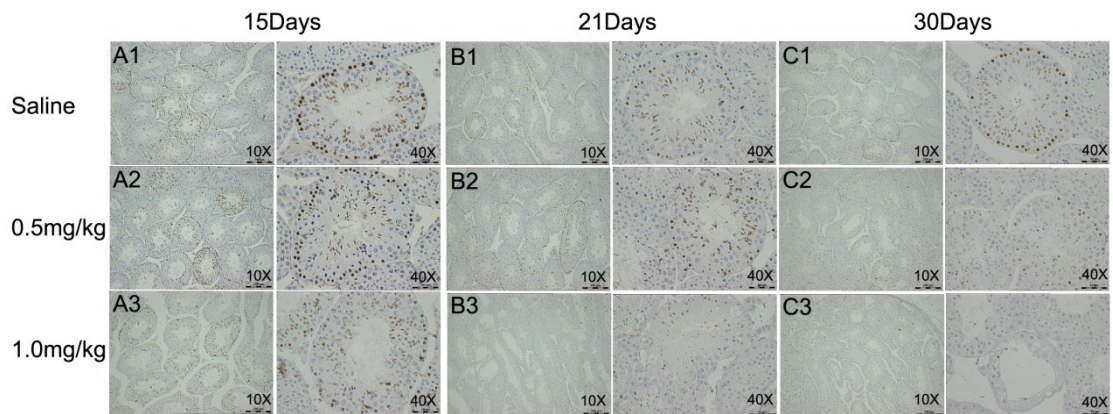


Fig. S5. LLDT-8 affected the expression of several MAPKs.

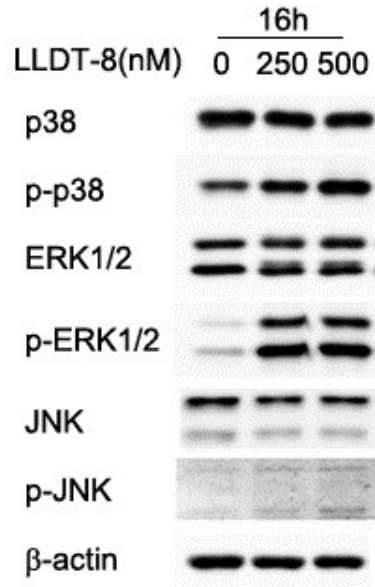


Fig. S6. Tak1 siRNA screening (A) and the effects of LLDT-8 on the transcription level of Tak1 in GC-2spd cells (B).

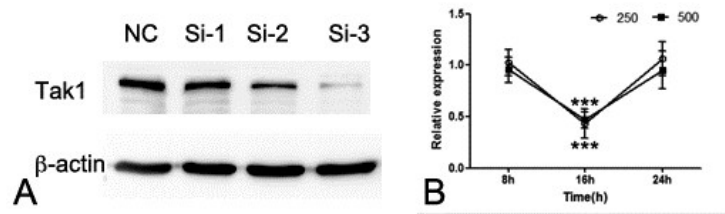


Fig. S7. The expression of RNA polymerase II was downregulated by LLDT-8 in GC-2spd.

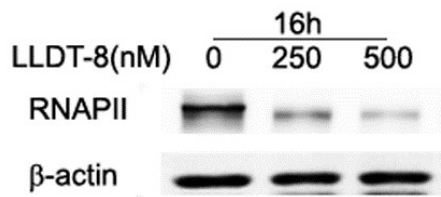


Fig. S8. Representative results.

