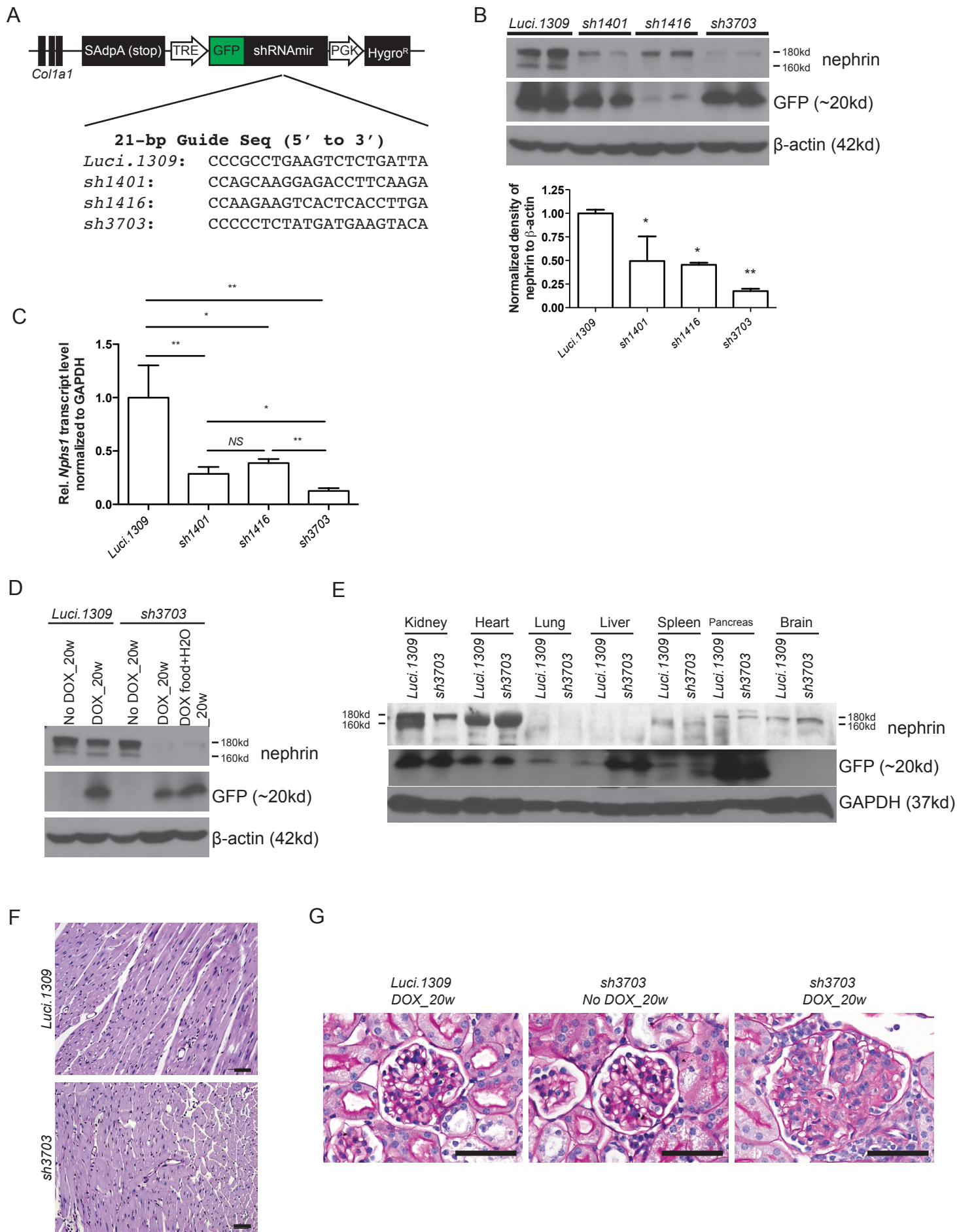
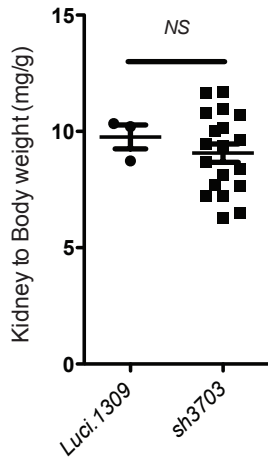


# Supplemental Figure 1

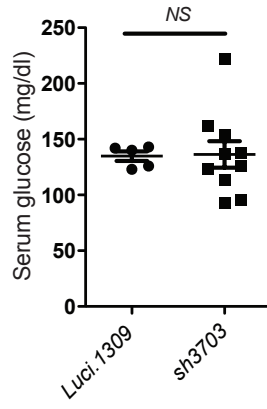


Supplemental Figure 2

A



B



## Supplemental Figure Legend:

**Supplemental Figure 1.** The expression of nephrin in three distinct lines of inducible nephrin knockdown mice. (A) A representative schema of the doxycycline (DOX)-inducible gene construct, *TGM*, which is inserted downstream of the endogenous *Col1a1* gene in the mouse genome. The transgene was configured with a tetracycline responsive element (TRE) that drives the expression of a fusion transcript containing the coding sequence of a green fluorescent protein (GFP) as well as a mir30-expression cassette (shRNAmir) that contains a 21-bp guide sequence targeting the gene of interest. Four different lines of inducible knockdown mice were used in the study. The *Luci.1309* mice have inducible expression of a guide sequence targeting the firefly luciferase. The *sh1401*, *sh1416* and *sh3703* lines of mice have inducible expression of three different guide sequences targeting different parts of the mouse *Nphs1* mRNA. (B) Representative western blots of kidney lysates from the indicated mice. Each lane is from protein lysate of a distinct mouse after 6 weeks of DOX induction. A bar graph of ratio of band density for nephrin/ $\beta$ -actin normalized to the *Luci.1309* sample. (C) Relative expression of the nephrin mRNA transcript in the kidney of the indicated group of mice normalized to the *Luci.1309* group. (D) Representative western blots for nephrin, GFP, and beta-actin for age-matched *luci.1309* and *sh3703* mice with and without DOX feeding (DOX vs. No DOX, respectively). To induce *sh3707* mice with a higher dose of DOX, they were fed with DOX in the chow and drinking water (i.e. DOX food+H<sub>2</sub>O<sub>20w</sub>). (E) Representative western blots for nephrin, GFP, and GAPDH in the indicated organs of *Luci.1309* and *sh3703* mice. \*P<0.05. \*\*P<0.01. (F) Representative images of PAS-stained paraffin-embedded sections of the myocardium. (G) Representative images of PAS-stained kidney sections of mice with and without DOX feeding. Scale bar, 50 $\mu$ m.

**Supplemental Figure 2.** Kidney to body weight ratio and serum glucose of mice with and without nephrin knockdown after 20 weeks of DOX induction. NS, not significant.