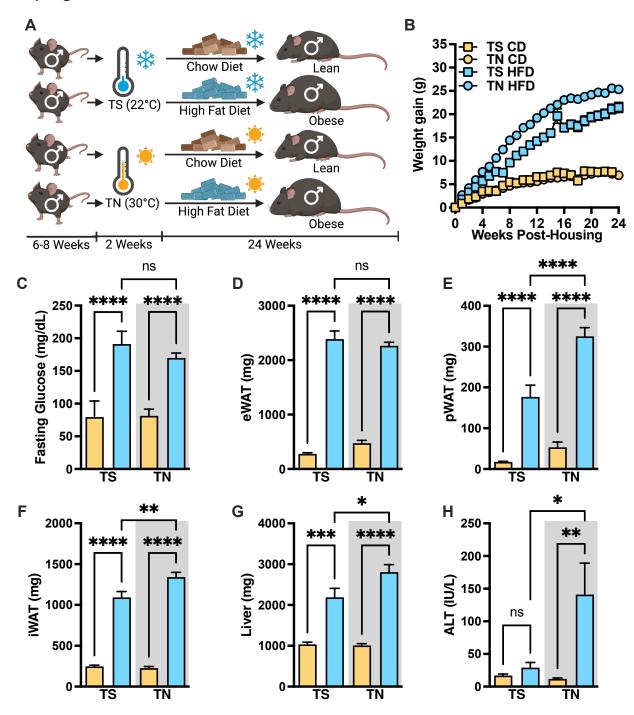
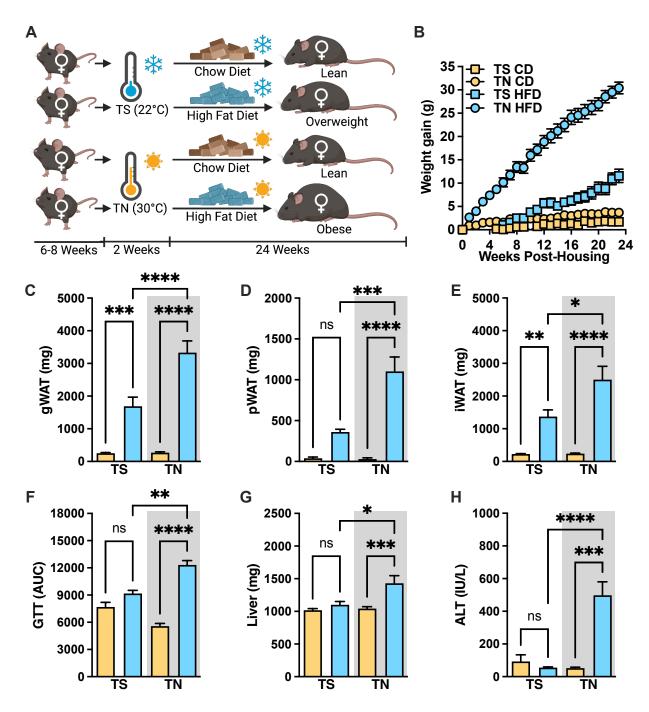


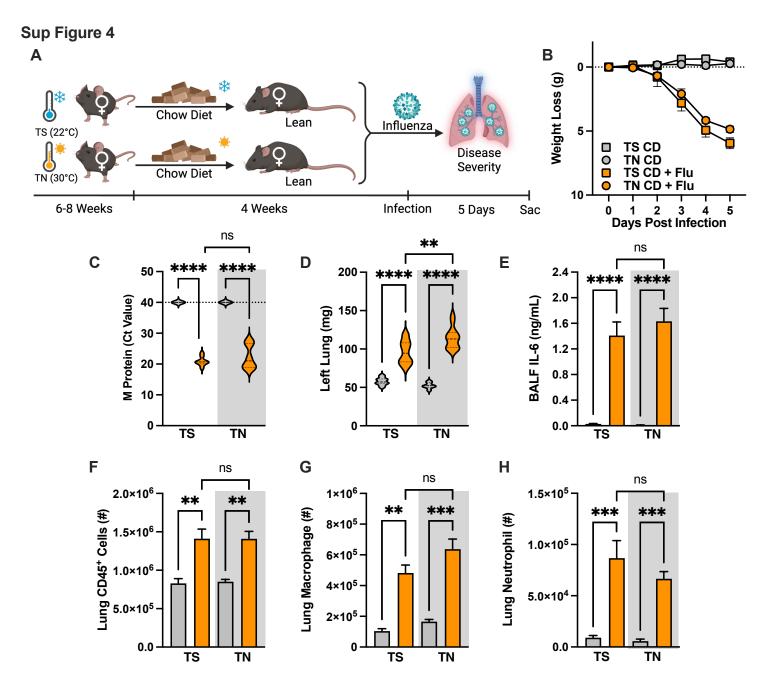
Supplemental Figure 1: Thermoneutral housing does not impact influenza disease severity in lean male mice. (A) C57BL/6 male mice (n=4-8/group; combined results of 2 experiments) were placed in either TS or TN housing and fed CD for 2-4 weeks during acclimatization to thermoneutral Caron chambers before challenge with influenza virus (30HA Units). (B) Weight loss post-infection. (C) Lung M Protein expression quantified via qPCR. (D) Left lung weight 5 days post-infection. (E) BALF IL-6 levels quantified via cytokine ELISA. (F) Total lung CD45<sup>+</sup> immune cell infiltration, measured by flow cytometry. (G) Lung macrophage absolute numbers (CD11b<sup>hi</sup>F4/80<sup>hi</sup>). (H) Lung Neutrophil absolute numbers (CD11b<sup>hi</sup>GR1<sup>hi</sup>). Means +/- SEM. Student's t Test or 1-way ANOVA; \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.



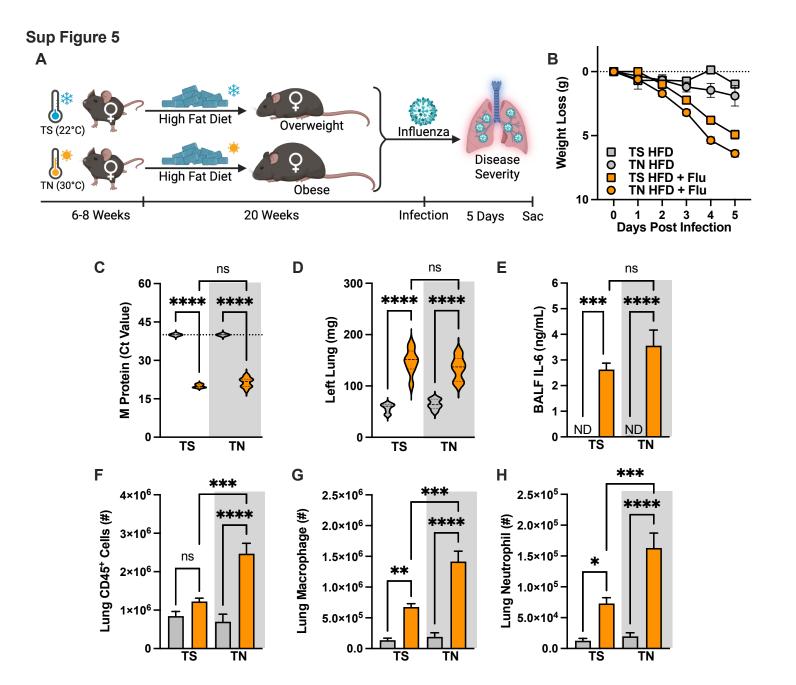
Supplemental Figure 2: Thermoneutral housing establishes a more robust model of diet-induced obesity in male mice. (A) 6–8-week-old C57BL/6 male mice (n=9-18/group; combined results of 3 experiments) were placed in either TS or TN housing and allowed to acclimate for 2 weeks. Subsequently, mice were placed on either CD or HFD for 24 weeks before harvest. (B) Weight gain. (C) Fasting glucose, measured on week 20 of diet. (E-F) Visceral White Adipose accumulation measured via gonadal/epididymal white adipose tissue (eWAT) and perirenal white adipose tissue (pWAT) weight at 23 weeks. (G) Subcutaneous White Adipose Tissue accumulation measured inguinal white adipose tissue (iWAT) weight at 23 weeks. (H) Liver weight at 23 weeks. (E) Hepatocellular damage measured by serum ALT at 23 weeks on diet. Means +/- SEM. Student's t Test or 1-way ANOVA; \*\*P<0.01.



Supplemental Figure 3: Thermoneutral housing establishes obesity and metabolic disease in female mice. (A) C57BL/6 female mice (n=6-15/group; combined results of 3 experiments) were placed in either TS or TN housing and fed either CD or HFD for 20 weeks before undergoing a glucose tolerance test (GTT). Mice were then allowed to gain weight for an additional 3 weeks before harvest. (B) Weight gain. (C-D) Visceral White Adipose accumulation measured via gonadal white adipose tissue (gWAT) and perirenal white adipose tissue (pWAT) weight at 23 weeks. (E) Subcutaneous White Adipose Tissue accumulation measured by inguinal white adipose tissue (iWAT) weight at 23 weeks. (F) Area under curve of GTT performed at week 20 of diet. (G) Liver weight at 23 weeks. (H) Hepatocellular damage measured by ALT at 23 weeks on diet. Means +/- SEM. Student's t Test or 1-way ANOVA; \*P<0.05, \*\*\*P<0.001, \*\*\*\*P<0.0001.



**Supplemental Figure 4: Thermoneutral housing does not impact influenza disease severity in lean female mice.** (A) C57BL/6 female mice (n=5-9/group; combined results of 3 experiments) were placed in either TS or TN housing and fed CD for 2-4 weeks during acclimatization to thermoneutral Caron chambers before challenge with influenza virus (30HA Units). (B) Weight loss post-infection. (C) Lung viral M protein expression quantified via qPCR. (D) Left lung weight 5 days post-infection. (E) BALF IL-6 levels quantified via cytokine ELISA. (F) Total lung CD45<sup>+</sup> immune cell infiltration, measured by flow cytometry. (G) Lung macrophage absolute numbers (CD11b<sup>hi</sup>F4/80<sup>hi</sup>). (H) Lung Neutrophil absolute numbers (CD11b<sup>hi</sup>GR1<sup>hi</sup>). Means +/- SEM. Student's t Test or 1-way ANOVA; \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.



Supplementary Figure 5: TN Housing and HFD-feeding exacerbates influenza disease severity in female mice. (A) Experimental design schema. 8-week-old WT C57/BL6 females (n=8-10/group; combined results of 3 experiments) were placed in TS or TN housing and fed HFD for 20 weeks before challenge with influenza virus (30HA Units). (B) Weight loss post-infection. (C) Lung viral M protein expression quantified via qPCR. (D) Left lung weight 5 days post-infection. (E) BALF IL-6 levels quantified via cytokine ELISA. (F) Total lung CD45<sup>+</sup> immune cell infiltration, measured by flow cytometry. (G) Lung macrophage absolute numbers. (H) Lung neutrophil absolute numbers. Means +/- SEM. Student's t Test or 1-way ANOVA; \*P<0.05, \*\*P<0.01, \*\*\*P<0.001, \*\*\*\*P<0.001.