Supplemental Figures

Figure S1

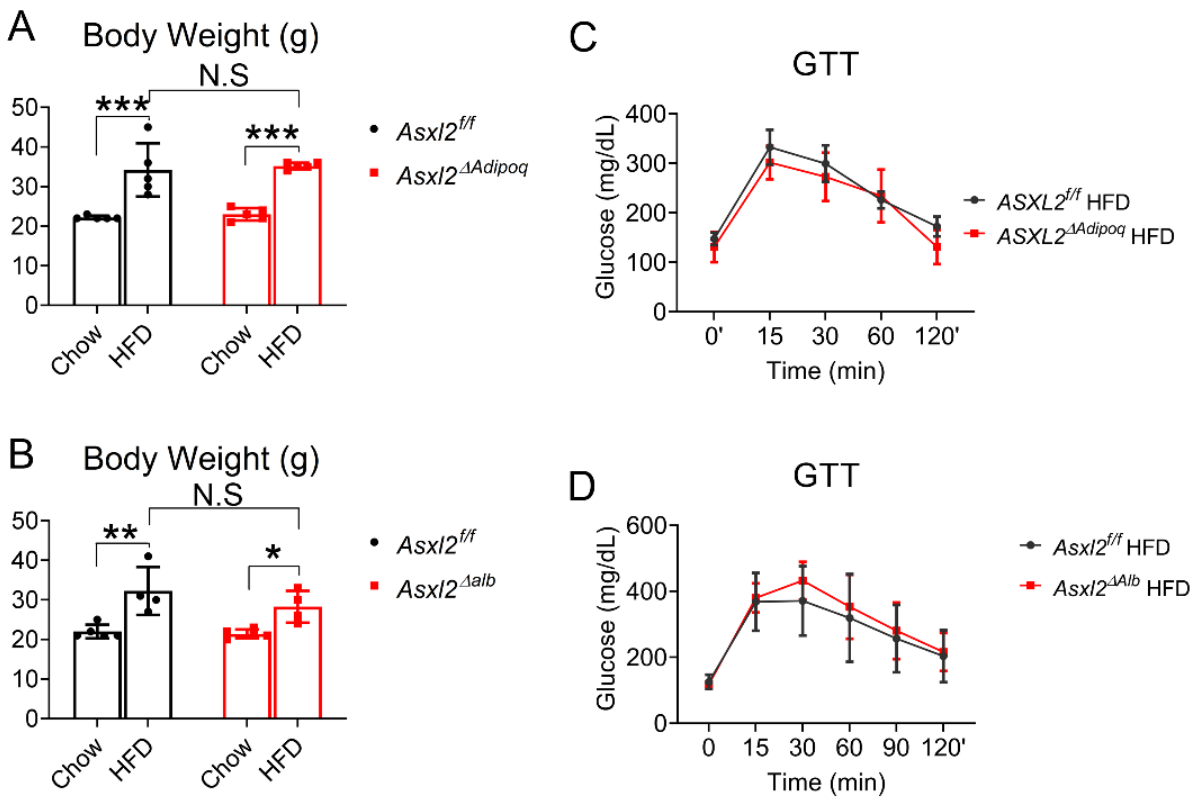

Fig S1: *Asxl2* deletion in adipose tissue or liver does not impact HFD-induced weight gain and glucose tolerance. A, B) Body weights of mice with selective deletion of *Asxl2* in A) adipose tissue or B) liver, fed chow diet or HFD for 8 weeks. C, D) Glucose tolerance test of mice with selective deletion of *Asxl2* in C) adipose tissue or D) liver, fed HFD for 8 weeks. Data are presented as mean ± SD. **p<0.01; *** p<0.001 as determined by 2 way ANOVA with Holm-Sidak's post hoc analysis for multiple comparisons test.

Figure S2

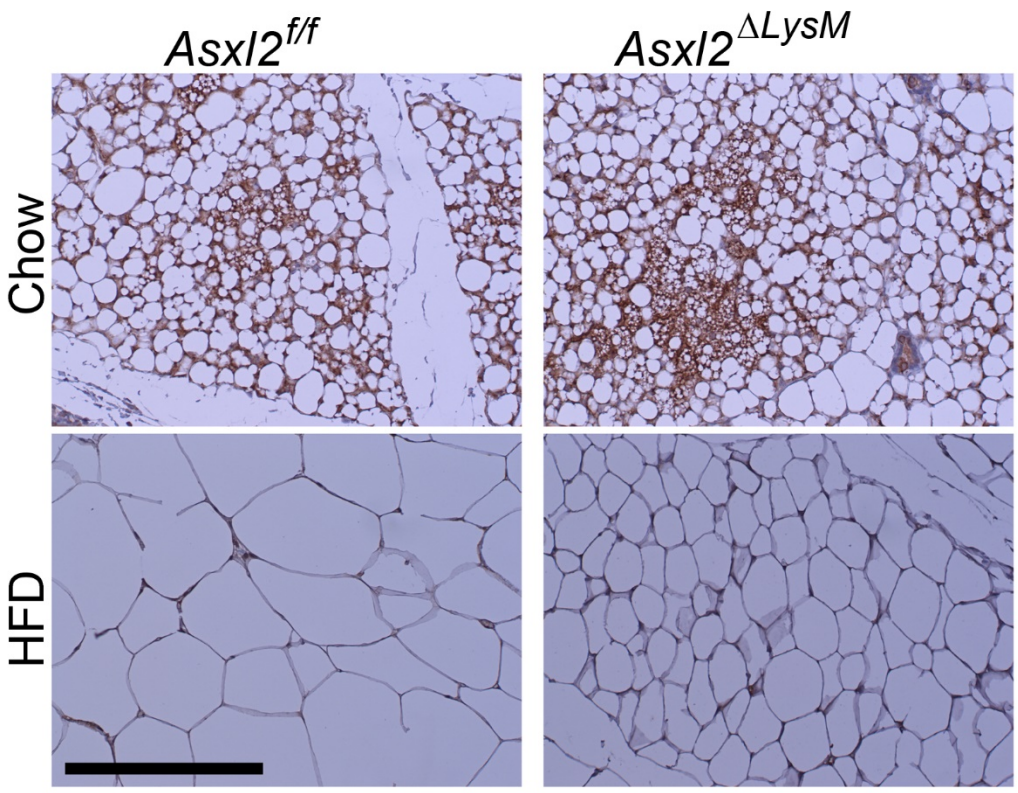

Fig S2: Beiging is not evident in WAT of *Asxl2*$^{\Delta LysM}$ mice fed HFD. Histological sections of inguinal WAT of *Asxl2*$^{f/f}$ and *Asxl2*$^{\Delta LysM}$ mice fed chow diet or HFD immunostained for UCP1; Scale bar: 200µm.

Figure S3

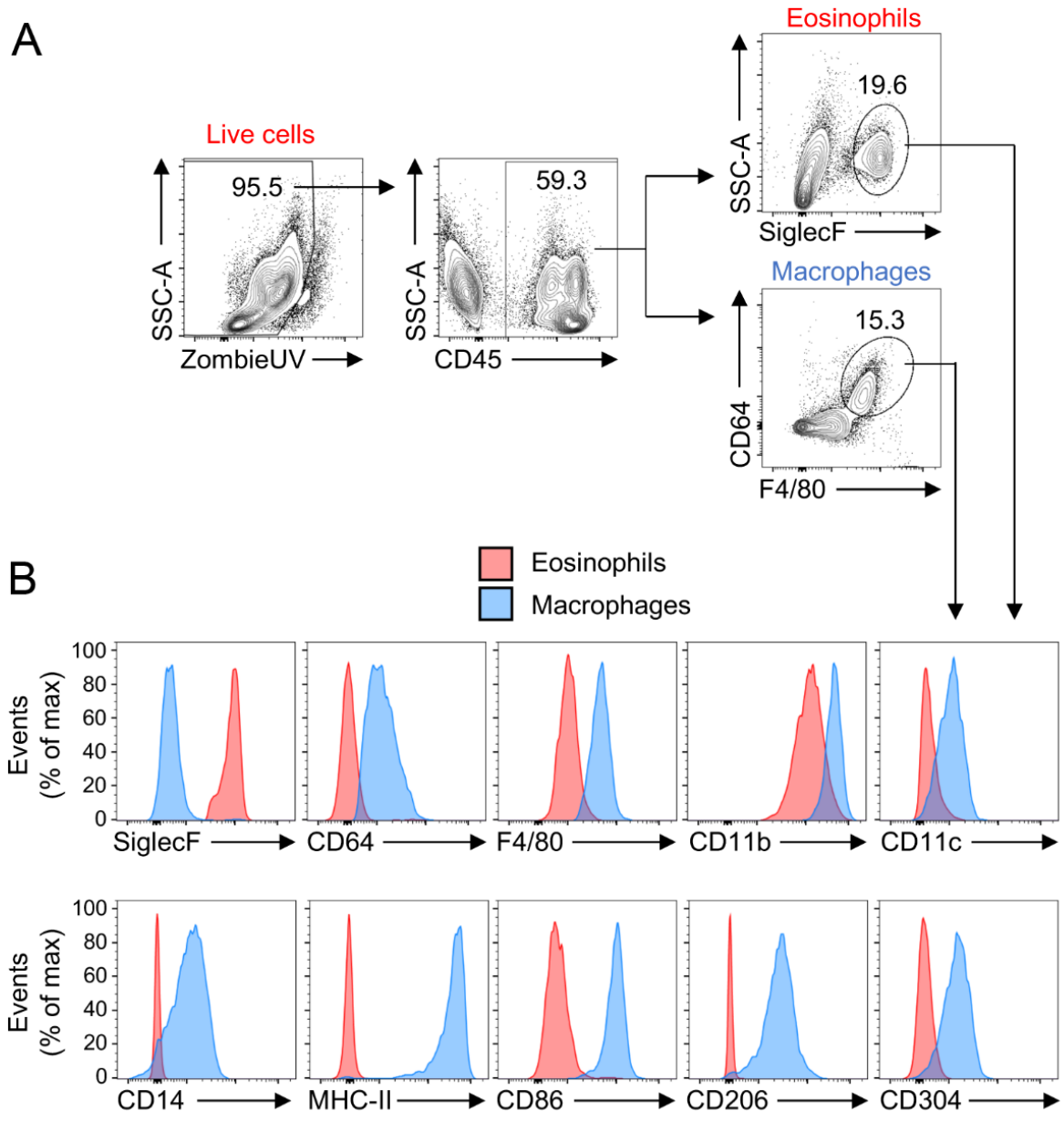

Fig S3: Identification of macrophages and eosinophils in adipose tissue. The stromal vascular fraction of gonadal adipose tissue of HFD- fed *Asxl2*$^{f/f}$ and *Asxl2*$^{\Delta LysM}$ mice was isolated and stained for flow cytometric analysis. A) Gating strategy to define SSC^{hi} SiglecF^{+} eosinophils (red) and F4/80^{+} CD64^{+} macrophages (blue). B) These eosinophil and macrophage populations were gated and overlaid to examine expression of the indicated surface markers.

Figure S4

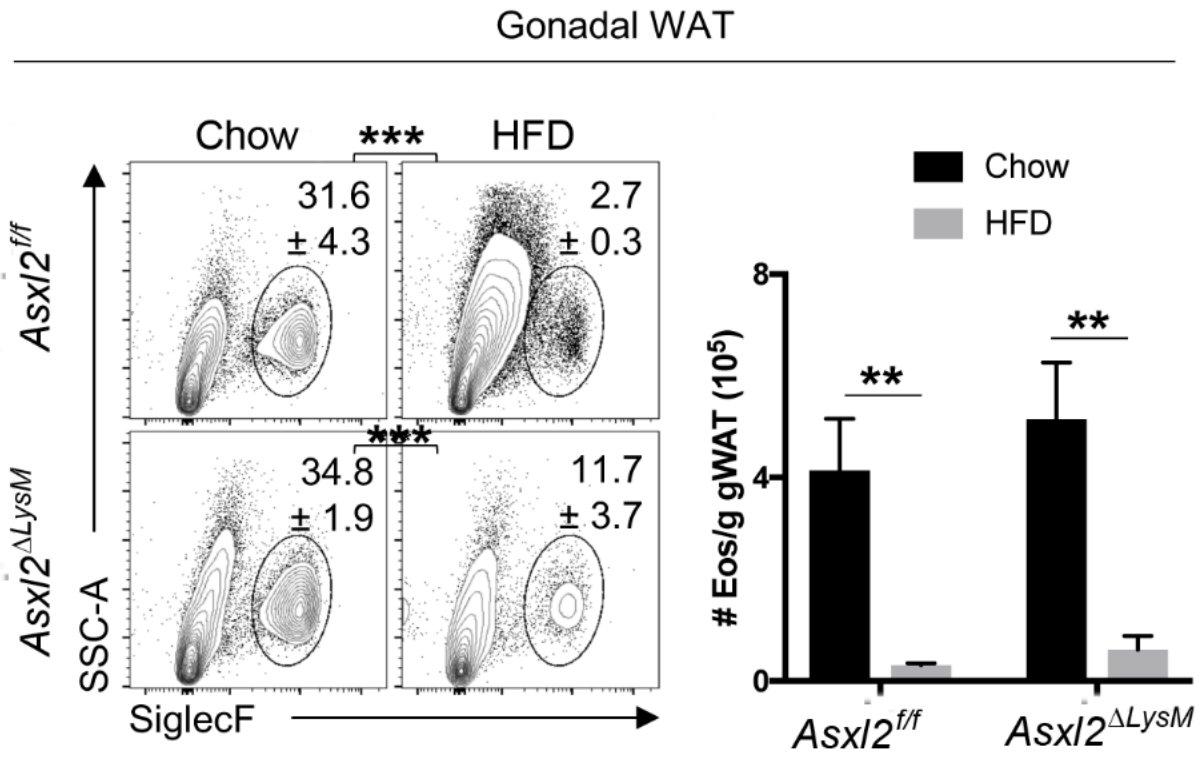

Fig S4: Eosinophils are decreased in obese gonadal WAT in an ASXL2-independent manner. Female *Asxl2*$^{f/f}$ and *Asxl2*$^{\Delta LysM}$ mice were fed either a chow diet or HFD for 8 weeks. A) Frequencies and B) numbers of SSC^{hi} SiglecF^{+} eosinophils in gonadal white adipose tissue (WAT). Pre-gated on singlet, live, CD45^{+} cells. Two-way analysis of variance with Tukey post-hoc test.

Figure S5

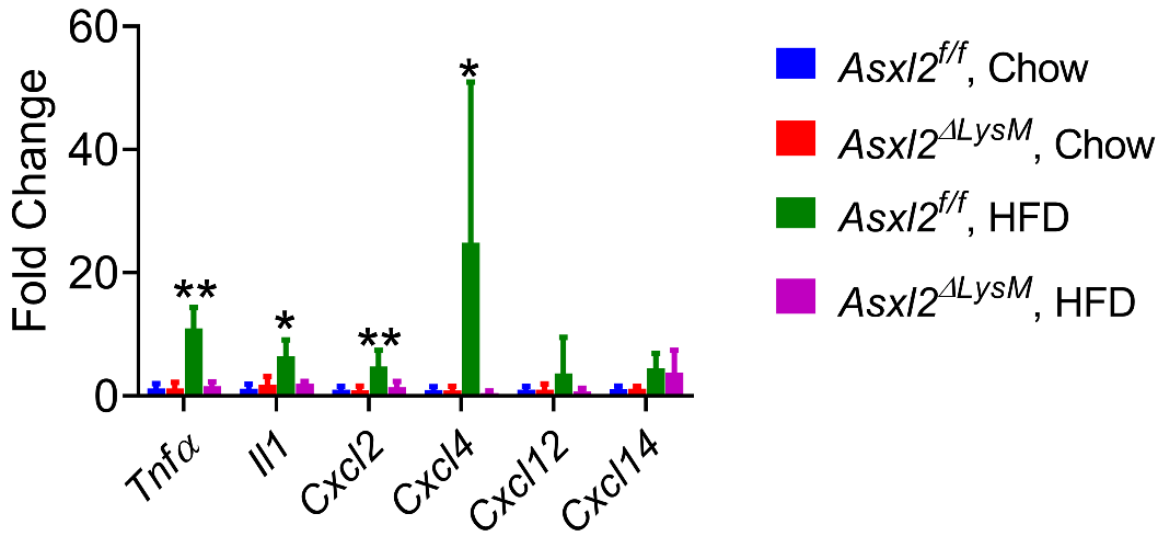

Fig S5: *Asxl2* expression in myeloid cells is required for macrophage accumulation in WAT and BAT in obesity. Inflammatory cytokine and chemokine mRNA expression in stromal vascular fraction of gonadal WAT of *Asxl2*$^{f/f}$ or *Asxl2*$^{\Delta LysM}$ mice after 8 weeks fed with Chow diet or HFD. Data are presented as mean ± SD. *p<0.05; **p<0.01; *** p<0.001 as determined 2 way ANOVA with Holm-Sidak's post hoc analysis for multiple comparisons test.

Figure S6

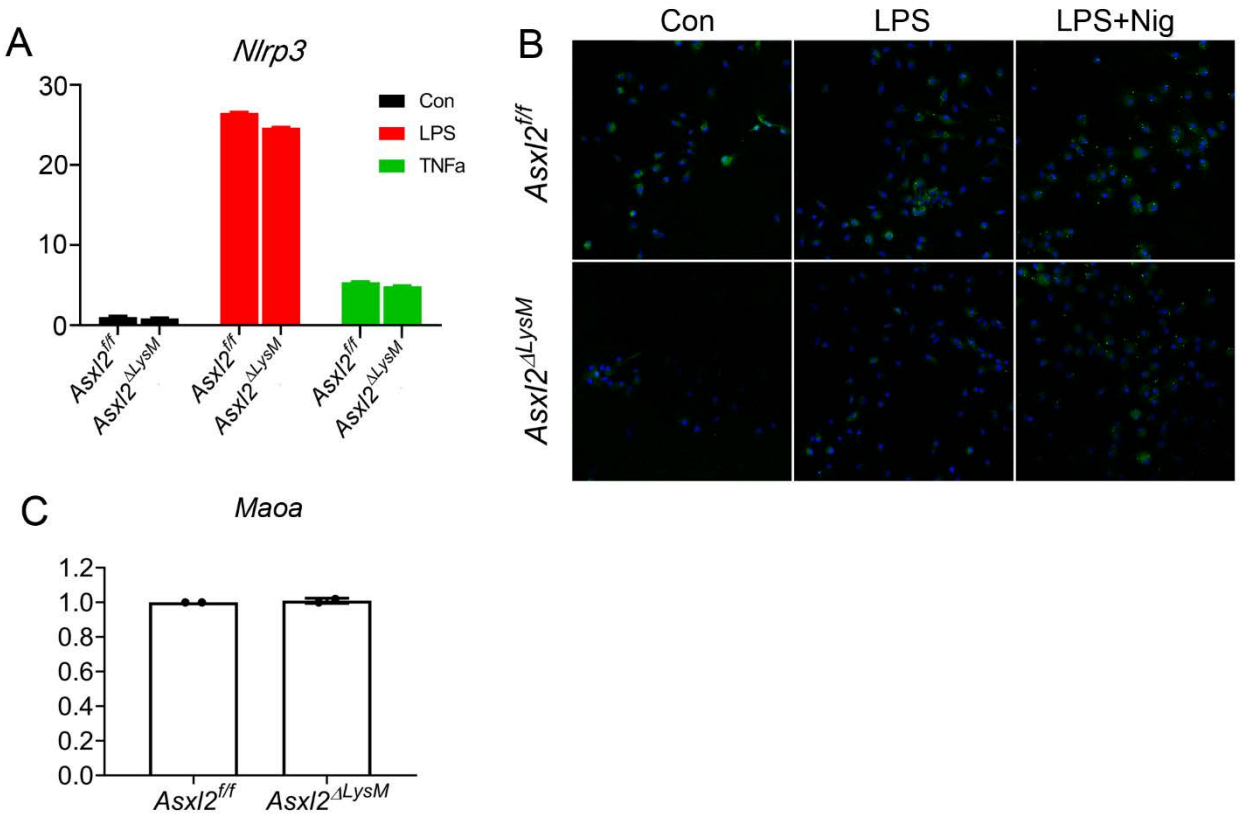

Fig S6: ASXL2 does not affect NLRP3 activation in macrophages. A) BMMs of *Asxl2*$^{f/f}$ and *Asxl2*$^{\Delta LysM}$ mice were stimulated with LPS (100ng/ml) or TNFa (10 ng/ml) for 3 hours, *Nlrp3* mRNA expression were measured by qPCR; B) *Asxl2*$^{f/f}$ or *Asxl2*$^{\Delta LysM}$ BMMc were incubated for 3 hours with 100 ng/ml LPS and stimulated with 15 µM nigericin for 30 minutes. Cells were then incubated with FLICA^{TM} FAM-YVAD-FMK probe and analyzed by fluorescence microscopy. C) *Maoa* mRNA abundance in BMMs of *Asxl2*$^{f/f}$ and *Asxl2*$^{\Delta LysM}$ mice were analyzed by qPCR. (n= 2 independent experiments).

Figure S7

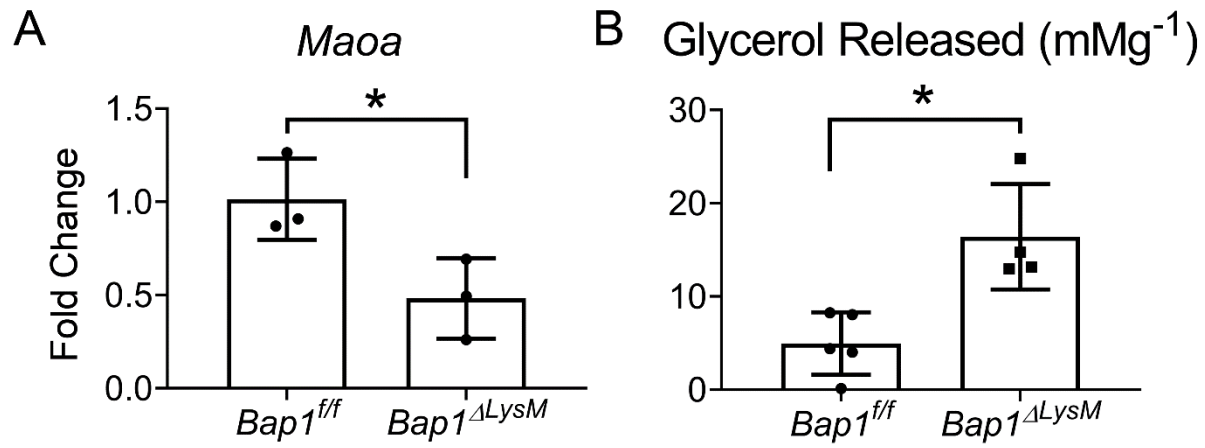

Fig S7: A) *Maoa* mRNA abundance in BAT stromal vascular fraction of HFD-fed control and *Bap1*$^{\Delta LysM}$ mice; B) Lipolysis analysis in BAT explants derived from HFD-fed control and *Bap1*$^{\Delta LysM}$ mice. Data are presented as mean ± SD. *p<0.05 as determined by unpaired t test.

Figure S8

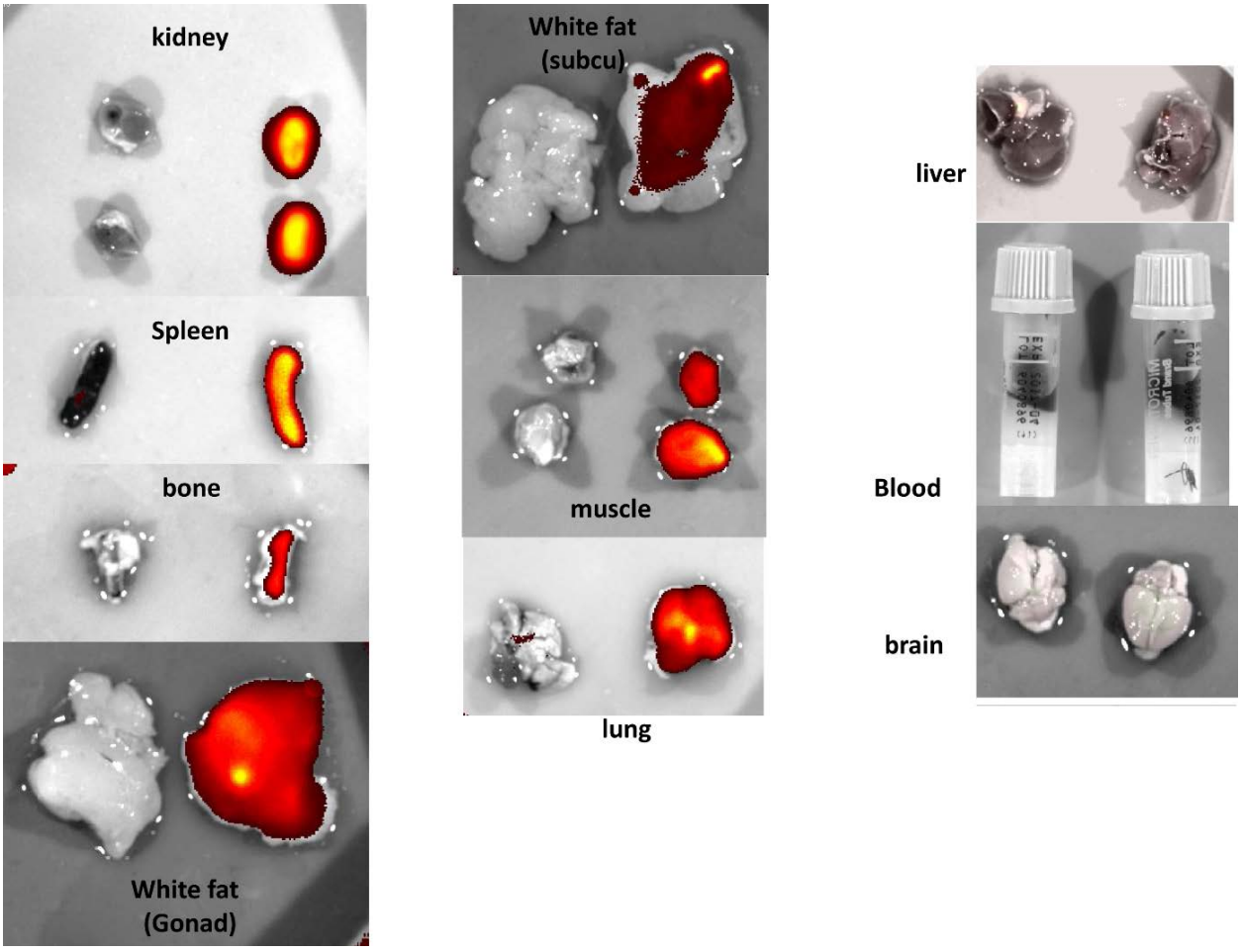

Fig S8: Nanoparticle-associated *Asxl2*-siRNA targets macrophages in numerous tissues. Fluorescent scan of organs of WT HFD-fed WT mice administered Cy5.5-labeled nanoparticle free (left) or nanoparticle- associated (right) *Asxl2*-siRNA