Supplementary Figure 1: Reciprocal BMTs demonstrate that hematopoietic  $Tlr4^{-l-}$  animals respond to high fat diet. WT and  $Tlr4^{-l-}$  C57Bl6/J male mice were irradiated at 8 weeks of age and then transplanted with marrow of the opposite genotype. WT marrow into  $Tlr4^{-l-}$  (WT $\rightarrow Tlr4^{-l-}$ ) vs  $Tlr4^{-l-}$  marrow into WT mice ( $Tlr4^{-l-} \rightarrow$ WT). 6 weeks after BMT animals were started on HFD and assessed after 16 weeks: (A) inguinal white adipose tissue (IWAT) weight, (B) % IWAT, (C) liver, (D) and spleen weight at 16 weeks of HFD. (H) GWAT adipocyte cross-sectional area distribution at 16 weeks of HFD. \*p<0.05. N=6-8 in WT $\rightarrow$ WT and  $Tlr4^{-l-} \rightarrow Tlr4^{-l-}$  and N=10-14 in WT $\rightarrow Tlr4^{-l-}$  and  $Tlr4^{-l-} \rightarrow$ WT groups.

Supplementary Figure 2: Reciprocal BMT leukocyte and progenitor populations. (A) Blood flow cytometry evaluations 2 weeks post BMT (N=6-14 in WT $\rightarrow$ *Tlr4<sup>-/-</sup>* and *Tlr4<sup>-/-</sup>* $\rightarrow$ WT groups). (B) GWAT quantitative RT-PCR gene expression (N=5-10 in WT $\rightarrow$ *Tlr4<sup>-/-</sup>* and N=6-8 in *Tlr4<sup>-/-</sup>* $\rightarrow$ WT groups). (C) Flow cytometry analysis of BM leukocytes (N=6 in WT $\rightarrow$ *Tlr4<sup>-/-</sup>* and N=8 in *Tlr4<sup>-/-</sup>* $\rightarrow$ WT groups) (D) myeloid progenitors (N=11 in WT $\rightarrow$ *Tlr4<sup>-/-</sup>* and N=13 in *Tlr4<sup>-/-</sup>* $\rightarrow$ WT groups), (E) spleen and (F) blood leukocytes populations after 16 weeks of HFD (N=6 in WT $\rightarrow$ *Tlr4<sup>-/-</sup>* and N=8 in *Tlr4<sup>-/-</sup>* $\rightarrow$ WT groups). \*p<0.05. \*\*p<0.01, \*\*\*p<0.001,

Supplementary Figure 3: Proliferation of ATM and DCs in WT and *Tlr4<sup>-/-</sup>* animals. (A) Gating scheme and representative flow cytometry plots from 12-week-old ND or 2 week HFD challenged WT and *Tlr4<sup>-/-</sup>* mice. WT and *Tlr4<sup>-/-</sup>* animals were started on HFD at 6 weeks of age for 16 weeks. After 16 weeks (A) GWAT and (B) IWAT leukocyte populations were evaluated for Ki67 by flow cytometry. \*p<0.05. \*\*p<0.01, \*\*\*p<0.005, \*\*\*\*p<0.001. N=11 WT ND, N=9-10 *Tlr4<sup>-/-</sup>* ND, N=11-12 WT HFD, and N=11-13 *Tlr4<sup>-/-</sup>* HFD.

Supplementary Figure 4: WT, *Tlr4<sup>-/-</sup>*, *Trif<sup>-/-</sup>* and *Myd88<sup>-/-</sup>* animals respond metabolically to HFD challenge. (A) 16 week fed insulin and (B) free fatty acids (FFA) and (C) liver triglycerides with (D) liver histology at 10 x (top panel) and 20 x (bottom panel). (N=12-16 in WT groups, N=10-11 in *Tlr4<sup>-/-</sup>* groups, N=7-9 in *Trif<sup>-/-</sup>*, and N=5-7 in *Myd88<sup>-/-</sup>*, for liver triglycerides N=1 WT, N=15 *Tlr4<sup>-/-</sup>* groups, N=3*Trif<sup>/-</sup>*, and N=8 in *Myd88<sup>-/-</sup>*) \*p<0.05. \*\*p<0.01, \*\*\*p<0.005, \*\*\*\*p<0.001. #p<0.05, ##p<0.01, ###p<0.005 when compared to WT ND or HFD control.



## **Supplementary Figure 1**



**Supplementary Figure 2** 

Α.

## **Supplementary Figure 3**



ATM 0-

COME COME FIN

Β.

WT ND

WT HFD TLR4-/- ND

TLR4-/- HFD

**GWAT % Ki67** 

50-

40

30

20

10

Α.

Unstained

C.

с с





Single stain control



D.



## **Supplementary Figure 4**