SUPPLEMENTARY DATA

Wound Histology. Wounds were excised from the backs of mice using a 6mm punch biopsy. sections were fixed in 10% formalin overnight before embedding in paraffin. 5μM sections were stained with hematoxylin and eosin for evaluation of re-epithelialization and inflammation and with Masson's Trichrome stain for collagen deposition. Images were captured using Olympus BX43 microscope and Olympus CellSens Dimension software. Percent re-epithelialization was calculated by measuring distance traveled by epithelial tongues on both sides of the wound divided by the total distance for full re-epithelialization.

RNA Analysis. Total RNA extraction was performed using Trizol (Invitrogen) according to manufacturer's instructions. RNA was then reversed transcribed to cDNA using iScript (Biorad). PCR was performed with 2X Taqman PCR mix using the 7500 Real-Time PCR System. Primers were purchased from Thermo-Fisher Scientific. Data was then analyzed relative to 18s ribosomal RNA ($2^{\Delta Ct}$). All samples were assayed in triplicate. Data was compiled in Microsoft Excel and presented using Prism software (GraphPad).

Chromatin Immunoprecipitation (ChIP) Assay. Briefly, cells fixed in paraformaldehyde were lysed and sonicated to generate 100-300bp fragments. To immunoprecipitate, samples were incubated in anti-H3K4trimethyl antibody (Abcam) or isotype control (rabbit polyclonal IgG) (Millipore) in parallel samples overnight followed by addition of proteinA Sepharose beads (Thermo-Fisher). Bound DNA was eluted and purified using Phenol:Chloroform:Isoamyl alcohol extraction and ethanol precipitation. qPCR was performed on enriched DNA samples as described below. Primers were designed using the Ensembl genome browser to search putative NFkB binding sites on gene promoters and then NCBI Primer-BLAST was used to design primers that flank those sites. The following primers were used to amplify DNA in samples: *IL1β*: 5' - GCAGGAGTGGGTGGGTGAGT– 3' and 5' – CAGTCTGATAATGCCAGGGTGC– 3', *Nos2*: 5' – GTCCCAGTTTTGAAGTGACTACG – 3' and 5' –GTTGTGACCCTGGCAGCAG– 3', *Tnfa*: 5' – TCCTGATTGGCCCCAGATTG – 3' and 5' – TAGTGGCCCTACACCTCTGT – 3'.

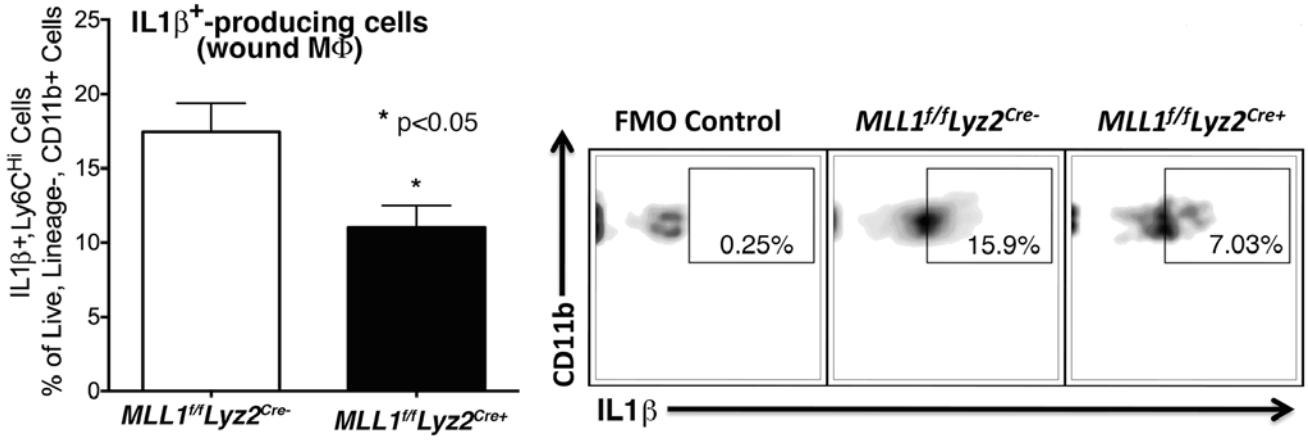
Bone Marrow Derived Macrophage Culture. After initial cell counting and plating in RPMI, FBS, L-cell supernatant, Glutamine, P/S cells were cultured for 6 days. Briefly, on day 6, cells were replated in triplicate ($3x10^5$cells/well). The next day, macrophages were stimulated with/without LPS(Sigma) for 2-24h. Cells were then placed in Trizol for qPCR or fixed for ChIP. For MLL1 inhibitor experiments, after 6-7 days of culture, $2x10^5$ BMDM per well were replated. Cells were treated with specific MLL1 inhibitor, MI-2 (Selleck Chemicals), for 24h. Next, 100ng/ml of LPS was used to stimulate cells for 2h. Trizol was then used to extract RNA for qPCR analysis.

Flow cytometry. Prior to flow cytometry, wound isolates from single cell suspensions were either surface stained directly or placed ex vivo in Teflon-coated wells for 2 hours for application of GolgiStop (1:2000) with/without LPS stimulation (100ng/mL). Cells were initially stained with Fixable LIVE/DEAD Viability Dye (Thermo-Fisher). The cells were then washed with PBS, resuspended in Flow buffer, and incubated with Fc-Block Anti-CD16/32 (BioXcell) for 10 minutes. Surface staining then commenced with the following antibodies: anti-CD3, anti-CD19, anti-NK1.1, anti-Ly6G, anti-CD11b, and anti-Ly6C (Biolegend). The cells were then washed and biotinylation was performed with streptavidin-APC or streptavidin-APC-Cy7 (Biolegend). Cells were acquired on the flow cytometer or fixed for intra-cellular staining with formalin (2% formaldehyde). After fixation, cells were permeabilized, washed and stained with the following intra-cellular antibodies: anti-IL1β (BD Biosciences), anti-TNFα (Biolegend), and anti-MLL1 (Novus). Cells were then washed and resuspended in flow buffer and acquired on the 3-Laser Novocyte flow cytometry (Acea Biosciences).

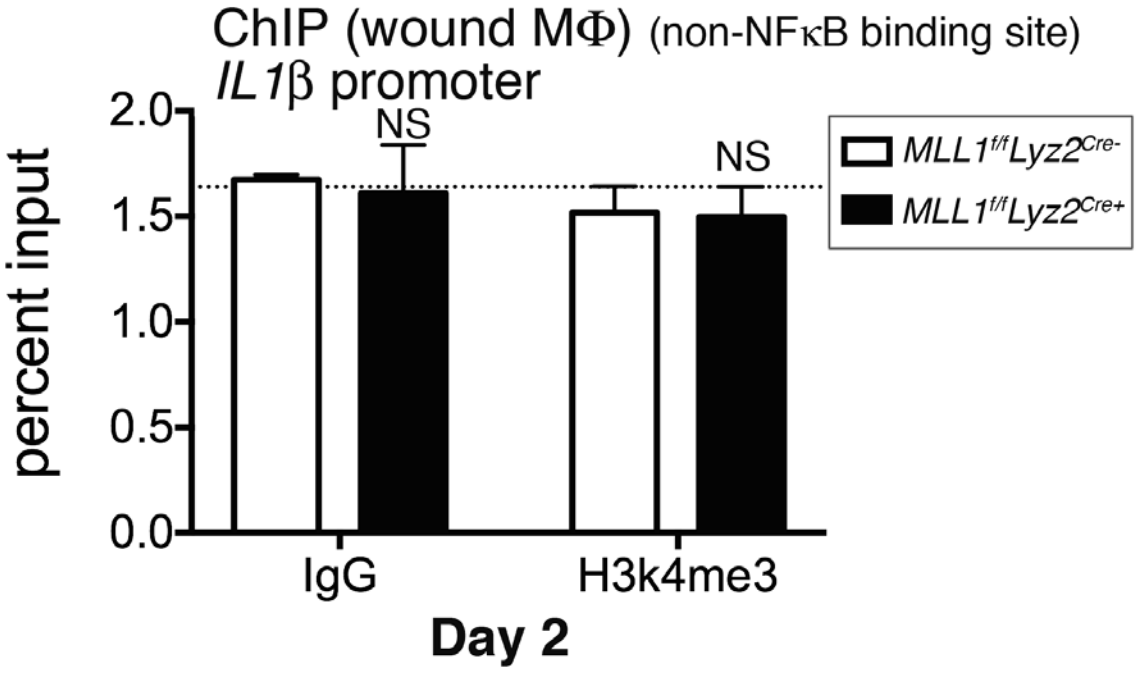
Immunoblotting. Cells were lysed and centrifuged at 12,000g for 15mins. Equal amounts of cell extracts were fractionated by SDS-PAGE and transferred to nitrocellulose membrane (Invitrogen). Membranes were incubated in primary antibodies (anti-IL1β; R&D and anti-b-Actin; Santa Cruz) overnight followed by horseradish peroxidase-conjugated anti-goat (Abcam) and visualized using enhanced chemiluminescent substrate (Thermo-Fisher).

SUPPLEMENTARY DATA

Supplementary Figure 1. Macrophages from *MLL1$^{f/f}$Lyz2^{Cre+}* wounds display decreased IL1β at day 5. *Mll1$^{f/f}$Lyz2^{Cre+}* and littermate control wound cell isolates were processed on day 5 for *ex vivo* intra-cellular flow cytometry following stimulation with LPS (100ng/mL) for 2 hours. The gating strategy used for *ex vivo* intra-cellular flow cytometry is shown in Figure 4. Density plots and histograms representing IL1β^{+}, Ly6C^{Hi} cells as a percent of live, lineage-, CD11b^{+} cells (*P< 0.05; n=10). Data are expressed as the mean +/- SEM.

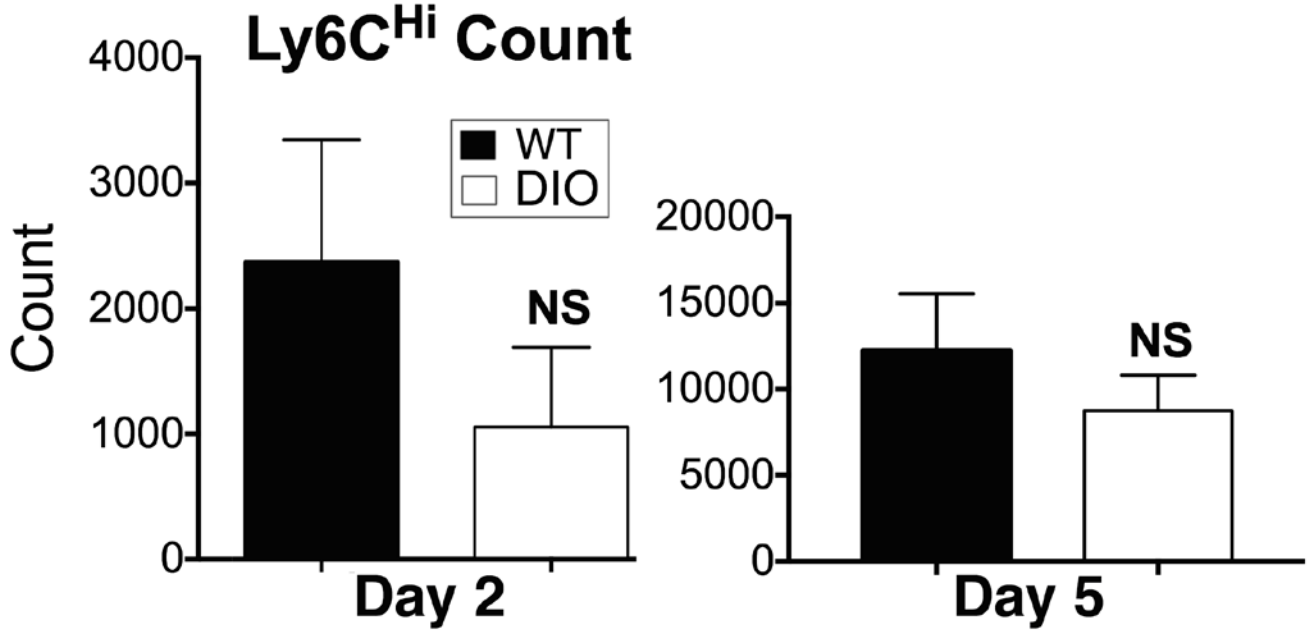


Supplementary Figure 2. *MLL1$^{f/f}$Lyz2^{Cre+}* wound macrophages do not display changes in H3K4me3 at non-NFκB binding sites. *MLL1$^{f/f}$Lyz2^{Cre+}* and littermate control wound macrophages CD11b^{+}[CD3^{-}, CD19^{-}, Ly6G^{-}] were MACs sorted from tissue at day 2 post-injury and processed for ChIP analysis. Primers were designed to target non-NFκB binding sites on the IL1β promoter. One representative primer set is shown. (NS = non-significant; n = 10, repeated 2x). Data are expressed as the mean +/- SEM.

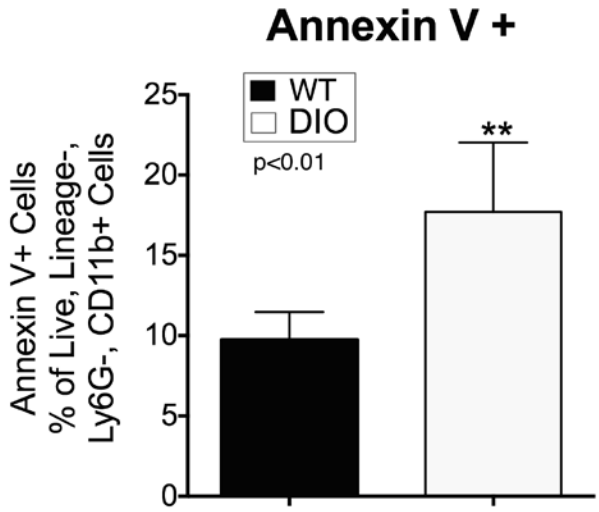


SUPPLEMENTARY DATA

Supplementary Figure 3. Ly6C^{Hi} macrophage accumulation does not differ in DIO and control wounds. DIO and control murine wounds were harvested following injury and wound cells were isolated. Single cell suspensions were processed for flow cytometry. DIO and control wound Ly6C^{Hi} macrophage counts were calculated from flow cytometry plots at days 2 and 5 post-injury (as gated in Figure 4) (NS = nonsignificant; n=10, repeated 1X). Data are expressed as the mean +/- SEM.



Supplementary Figure 4. DIO wound macrophages are more prone to apoptosis than controls. DIO and control murine wounds were harvested following injury and wound cells were isolated. Single cell suspensions were processed for flow cytometry. DIO and control wound macrophages were harvested on day 5 following injury and processed for flow cytometry viability staining with Annexin V. Histograms representing Annexin V staining cells as a percent of live, lineage-, Ly6G-, CD11b+ cells are shown (**P < 0.01; n=10). Data are expressed as the mean +/- SEM.



SUPPLEMENTARY DATA

Supplementary Figure 5. H3K4me3 at the NFκB binding site on the NOS2 promoter is decreased early and increased late in DIO wound macrophages. DIO and control wound macrophages $CD11b^{+}[CD3^{-}, CD19^{-}, Ly6G^{-}]$ were isolated from tissue at days 2 and 5 post-injury by MACs sorting. ChIP analysis of DIO and control wound macrophage H3K4me3 at the NFκB binding site on the NOS2 promoter (**P < 0.01; n=12, repeated 2X). Data are expressed as the mean +/- SEM.