Supplementary Data

BRG1 defines a genomic subset of inflammatory genes transcriptionally controlled by the glucocorticoid receptor

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Supplementary Figures S1 - S5

Supplementary Figure 1. GR interacts with SWI/SNF complex

Supplementary Figure 2. BRG1 ChIP-seq in macrophages (LPS and LPS+Dex)

Supplementary Figure 3. ATAC-seq in primary macrophages

Supplementary Figure 4. Loss of BRG1 affects GR function in macrophages

Supplementary Figure 5. Macrophage BRG1 and HDAC inhibition

Supplementary Tables S1 - S5

Supplementary Table S1: qRT-PCR primers

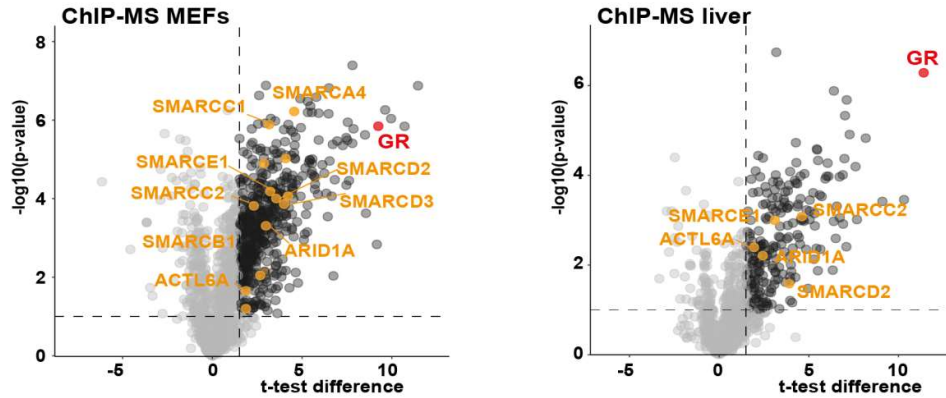Supplementary Table S2: ChIP-qPCR primers

Supplementary Table S3: Differentially expressed genes (BMDMs, *siBRG1*, LPS+Dex)

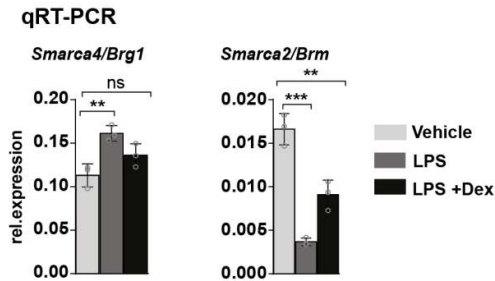Supplementary Table S4: Gene ontology annotation of various gene sets

Supplementary Table S5: Macrophage GR & BRG1 ChIP-seq plus ATAC-seq peaks
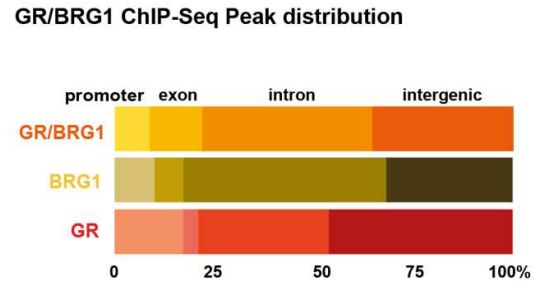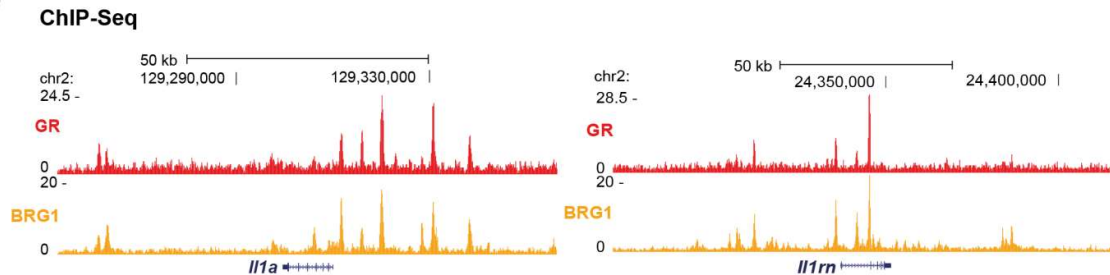
Supplementary Figure 1

A

B

qRT-PCR

C

GR/BRG1 ChIP-Seq Peak distribution

D

ChIP-Seq

Supplementary Figure 1. GR interacts with SWI/SNF complex. (A) GR ChIP-MS interactomes including subunits of the SWI/SNF chromatin remodeling complex from mouse embryonic fibroblasts (MEFs stimulated with LPS and Dex) and from mouse livers. (Quagliarini et al. 2019; Escoter-Torres et al. 2020) SWI/SNF components are marked in orange. (B) qRT-PCR of *Smarca4/Brg1* and *Smarca2/Brm* in vehicle, LPS and LPS plus Dex stimulated macrophages. Bars = mean ± standard deviation, ns = not significant, unpaired two-tailed Student's t-test, n=3. (C) Genomic feature distribution of GR and BRG1-bound sites and regions specifically occupied by either BRG1 and/or GR. ChIP-seq peak sets as in Fig. 1C. (D) Example genome browser tracks for *Il1a* and *Il1rn* loci showing the mean signal from two GR and BRG1 ChIP-seq replicates in LPS plus Dex treated macrophages (n=2).
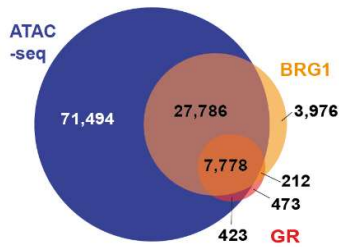
Supplementary Figure 2

A

BRG1 ChIP-seq

LPS

24,330   15,422

4,706

LPS+Dex

B

BRG1 ChIP-seq peak distribution

LPS

LPS+Dex

0   25   50   75   100 %

- promoter
- 5' UTR
- 3' UTR
- 1st exon
- other exon
- 1st Intron
- other intron
- downstream
- distal intergenic

C

ChIP-seq motif BRG1 LPS	Factor	E-value
AAAGGAAG	PU.1	3.2e-176
TGAGTCA	AP-1	4.3e-035
GGGGGGGGGGGG	SP1	3.7e-022

ChIP-seq motif BRG1 LPS+Dex	Factor	E-value
AAAGGAAGT	PU.1	1.5e-102
GGGTGGGGGGGGG	SP1	9.1e-022
TGACTCA	AP-1	1.1e-015

D

Gene Ontology

Gene Ratio
- 0.015
- 0.020
- 0.025
- 0.030
- 0.035
- 0.040

reg. of cell-cell adhesion
pos. reg. of cytokine production
small GTPase med. signal transduction
pos. reg. of response to ext. stimulus
actin filament organization
myeloid leukocyte activation
neg. reg. of immune system process
response to peptide
myeloid cell differentiation
leukocyte migration
reg. of T cell activation
pos. reg. of protein kinase activity
response to oxidative stress
response to INF-γ
reg. of leukocyte proliferation
reg. of protein cont. complex assembly
ERK1/2 cascade
reg. of cell shape
process utilizing autophagic mechanism
reg. of metal ion transport
mononuclear cell proliferation
calcium ion homeostasis
response to wounding
reg. of actin filament-based process
reg. of hemopoiesis
pos. reg. of secretion by cell
cell junction assembly
cellular response to LPS
pos. reg. of cell projection organization
neg. reg. of phosphorylation

adj. p value
- 0.005
- 0.010
- 0.015
- 0.020

Common   LPS   LPS+Dex
(7,263)   (2,074)   (6,854)

E

LPS   LPS+Dex

50 kb

chr2:   129,290,000   129,330,000

24.5 -
GR
0

20 -
BRG1
0

20 -
BRG1
0

Il1a

50 kb

chr2:   24,350,000   24,400,000

28.5 -
GR
0

20 -
BRG1
0

20 -
BRG1
0

Il1rn

Supplementary Figure 2. BRG1 ChIP-seq in macrophages treated with LPS and with LPS plus Dex. (A) Overlap of BRG1 binding sites in macrophages treated with LPS plus Dex (n=2) or with LPS only (n=2). (B) Genomic feature distribution of BRG1-bound sites for both conditions. (C) MEME motif enrichment of BRG1 ChIP-seq peaks. Motifs were filtered for E<0.01. (D) Enrichment for biological processes of genes associated with nearby BRG1 binding sites, for common (orange) or unique (either LPS or LPS plus Dex) macrophage peaks. neg. = negative, pos. = positive, reg. = regulation (E) Representative genome browser tracks for *Il1a* and *Il1rn* loci showing the mean signal of GR and BRG1 ChIP-seq in macrophages (n=2 each).

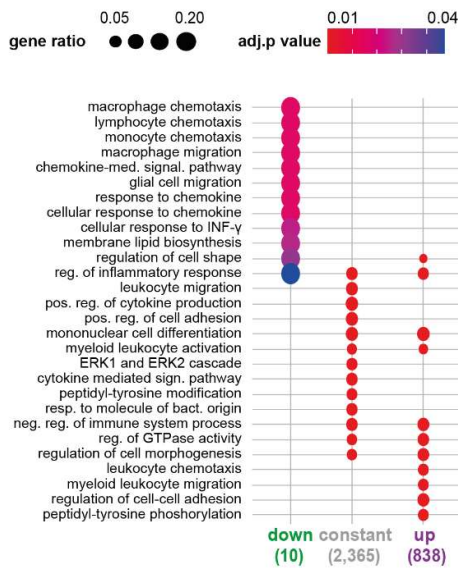## Supplementary Figure 3

A   peak overlap LPS+Dex

B

ATAC-seq motif LPS	Factor	E-Value
	PU.1	3.4e-060
	CTCF	1.5e-053

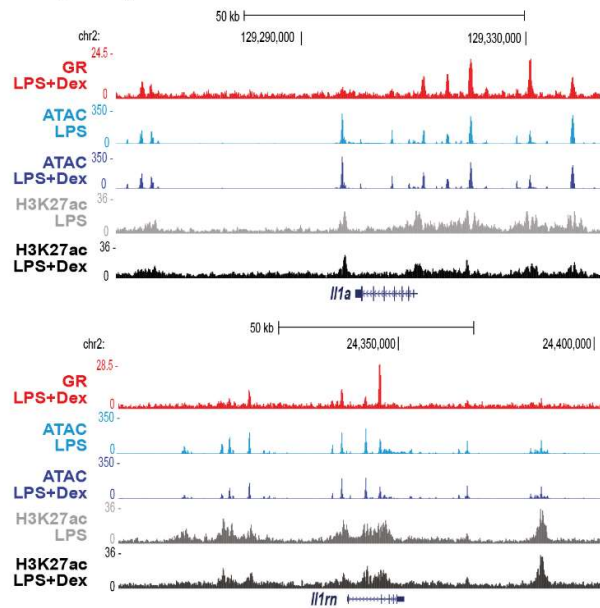| ATAC-seq motif LPS+Dex	Factor	E-Value
	CTCF	2.1e-040
	PU.1	2.6e-034
	AP-1	2.9e-007

C   ATAC-seq functional annotation

D   sequencing tracks

Supplementary Figure 3. ATAC-seq in macrophages responding to LPS or LPS plus Dex. (A) Overlap of accessible regions (ATAC-seq, n=4) with the BRG1 (n=2) and GR (n=2) binding sites, as determined by ChIP-seq in LPS+Dex treated macrophages. (B) MEME motif enrichment for the macrophage ATAC-seq peaks. Motifs were filtered for E<0.01. (C) Gene Ontology enrichment (biological process) of genes associated with the three categories of ATAC-seq peaks shown in Fig. 3B. cell. = cellular, neg. = negative, pos. = positive, reg. = regulation, resp. = response. (D) Representative genome browser tracks for *Il1a* and *Il1rn* loci showing mean ATAC-seq (n=4), GR (n=2) and H3K27ac ChIP-seq (n=2) coverage.
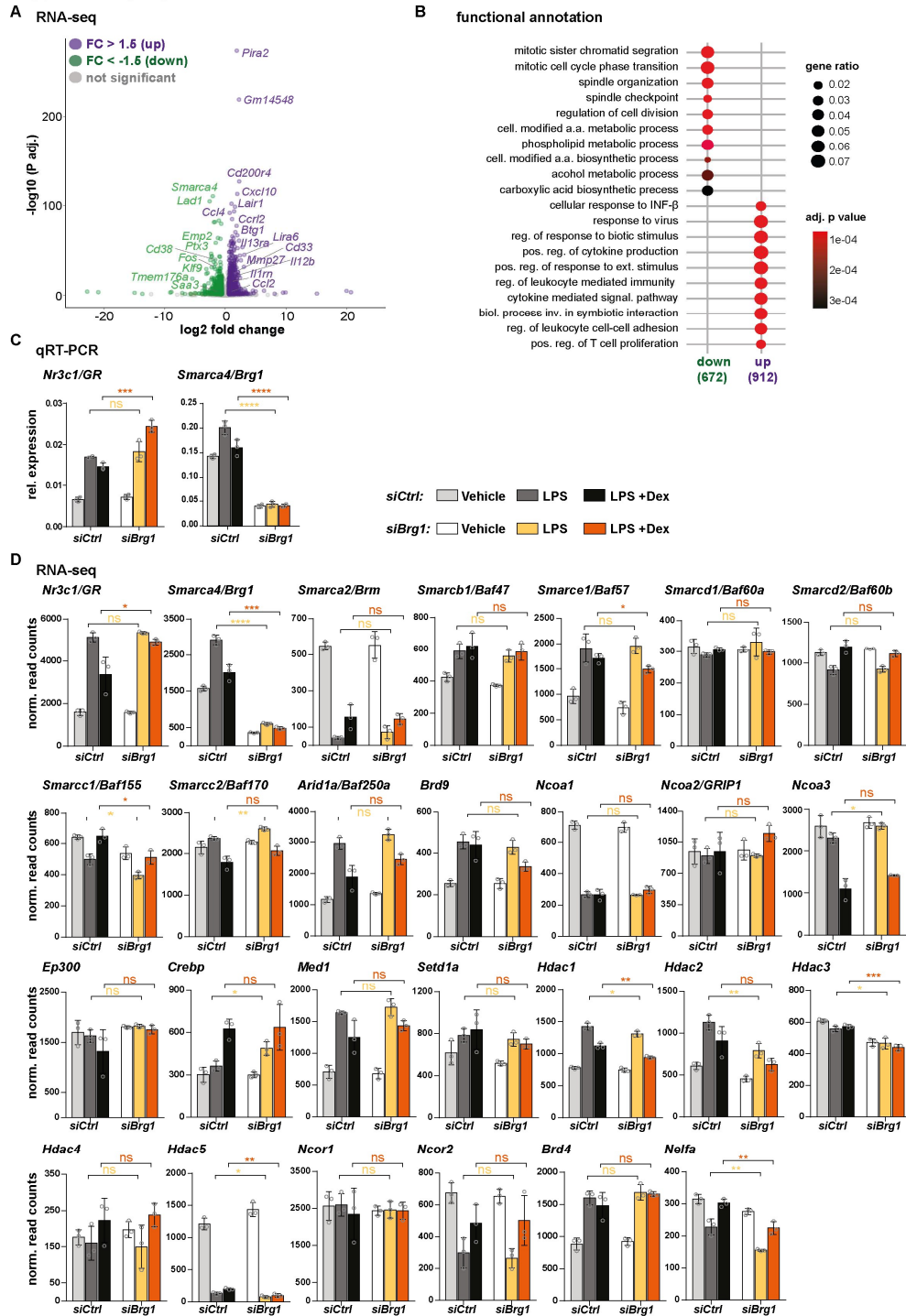
Supplementary Figure 4. *Brg1* knockdown affects macrophage gene expression. (A) Transcripts with differential expression between control and *Brg1* knockdown macrophages upon LPS+Dex treatment. (n=3, fold change ±1.5, p adjusted <0.05). (B) Gene Ontology enrichment for 'biological process' of differentially regulated genes in A. (C) qRT-PCR for *GR* and *Brg1* in control and *Brg1* knockdown macrophages. (D) DESeq-normalized RNAseq read counts for relevant factors in control and *Brg1* knockdown macrophages. For all bar graphs, values are means ± standard deviation. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, ns= not significant, unpaired two-tailed Student's t-test, n=3.
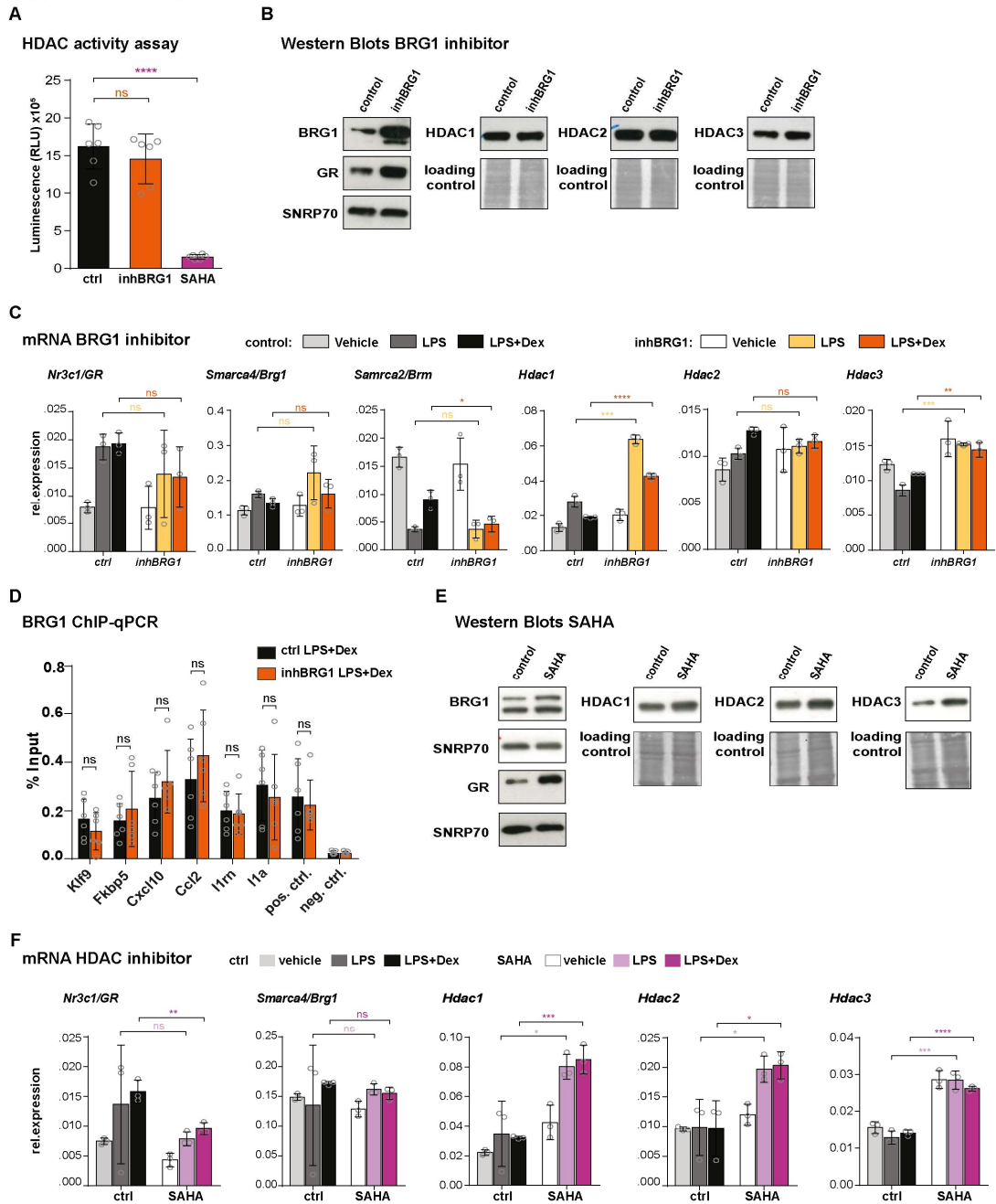
Supplementary Figure 5. BRG1 and HDAC inhibition in primary macrophages (A) HDAC activity assay in LPS+Dex stimulated macrophages treated with control, BRG1 inhibitor or SAHA. (B) Western blot showing nuclear BRG1, GR, HDAC1, HDAC2 and HDAC3 protein levels in control and BRG1 inhibitor treated macrophages (LPS+Dex). SNRP70 blotting and Naphthol Blue Black staining serve as loading control. (C) qRT-PCR of *GR, Brg1, Brm, Hdac1, Hdac2* and *Hdac3* in vehicle, LPS and LPS+Dex stimulated macrophages treated with vehicle (DMSO) or BRG1 inhibitor. (D) BRG1 ChIP-qPCR in LPS+Dex stimulated macrophages treated with vehicle (DMSO) or BRG1 inhibitor. (E) Western blot of nuclear BRG1, GR, HDAC1, HDAC2 and HDAC3 protein levels in control and SAHA treated macrophages (LPS+Dex). Loading controls: same as above. (F) qRT-PCR of *GR, Brg1, Brm, Hdac1, Hdac2* and *Hdac3* in vehicle, LPS and LPS+Dex stimulated macrophages treated with vehicle (DMSO) or SAHA. For all bar plots, values are mean ± standard deviation. *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001, ns= not significant, unpaired two-tailed Student's t-test, n= 3.