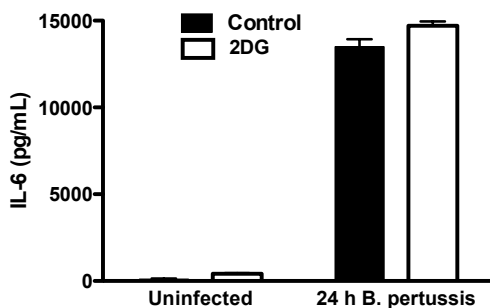
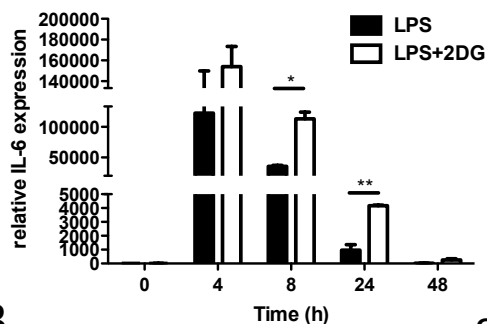
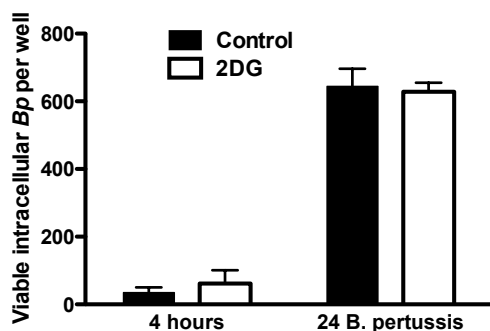


S1

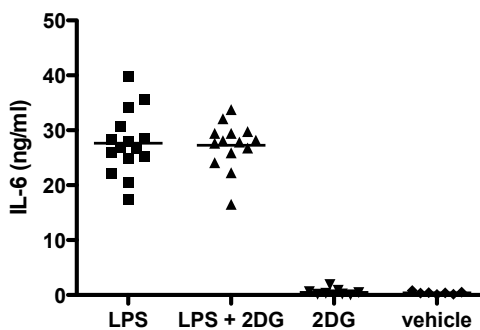
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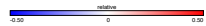
S3



S4

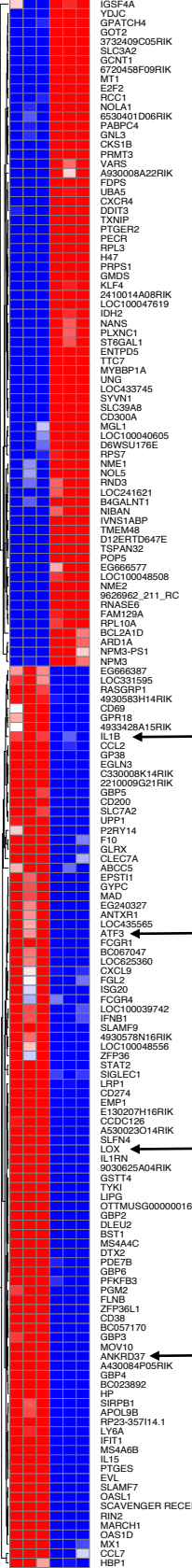


S1. LPS-or S2. *B pertussis*- induced IL-6 in BMDMs pretreated  $\pm$  2DG (1mM) for 3 h. S3. Bacterial CFU of *B pertussis* treated BMDMs were calculated following four days incubation at 37°C . S4. IL-6 in serum of mice i.p. injected  $\pm$  2DG (2g/kg) or PBS for 3 h, then LPS or PBS solution for 1.5 h. LPS n=15; LPS+2DG n=14; 2DG n=8; vehicle n=5. Error bars  $\pm$  s.e.m, \*  $p < 0.05$ .



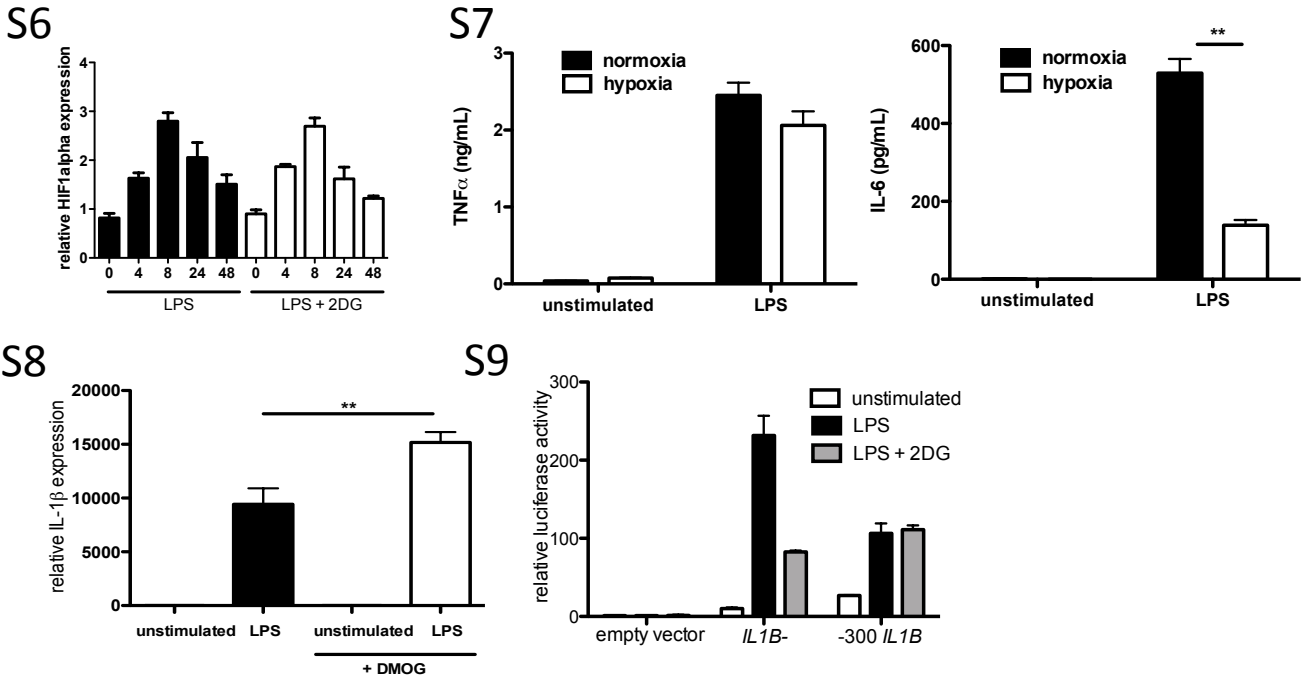
WT1\_LPS\_24h  
 WT2\_LPS\_24h  
 WT3\_LPS\_24h  
 WT1\_LPS\_2DG\_24h  
 WT2\_LPS\_2DG\_24h  
 WT3\_LPS\_2DG\_24h

Annotation



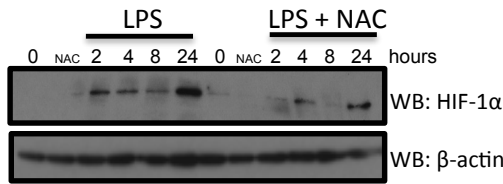
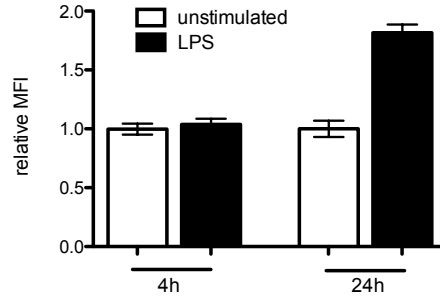
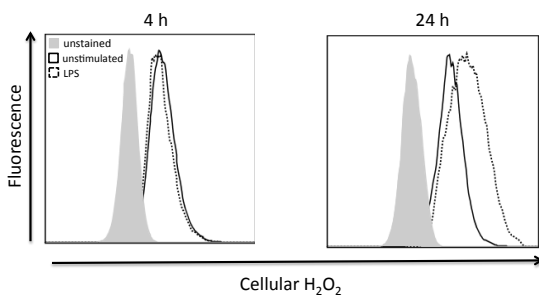
S5. Heat map representing genes regulated at 24 h by LPS that were both induced (red) and repressed (blue) by 2DG in BMDMs. n=3

IGSF4A  
 YDJC  
 GPAT4CH4  
 GOT2  
 3732409C05RIK  
 SLC3A2  
 GCNT1  
 6720458F09RIK  
 MT  
 E2F2  
 FCC1  
 NOLA1  
 6530401D06RIK  
 F48P64  
 GNL3  
 CKS1B  
 PRMT3  
 VARS  
 A83008A22RIK  
 FDP5  
 UBA5  
 CXCR4  
 DDI3  
 TXNIP  
 FTGER2  
 PEER  
 HLF3  
 HLF  
 PRPS1  
 GMD5  
 KLF4  
 2410014A08RIK  
 LOC10047619  
 IDH2  
 NANS  
 FLNCL1  
 ST6GAL1  
 ENTDP5  
 TTC7  
 MYBBP1A  
 UNG  
 LOC433745  
 SYVN1  
 SLC8A8  
 CD300A  
 MGL1  
 LOC100040605  
 DBWSU176E  
 RPS7  
 NME1  
 NOL5  
 FNDC3  
 LOC241621  
 B4GALNT1  
 NIBAN  
 IVNS1ABP  
 TME3A6  
 D12ERTD847E  
 TSPAN32  
 POF5  
 EG666577  
 LOC100048508  
 NME2  
 9626962\_211\_RC  
 RNASEL6  
 FAM129A  
 RPL10A  
 BCL2A1D  
 ARD1A  
 NPM3-PS1  
 NPM3  
 EG666387  
 LOC331585  
 RASGRP1  
 4930583H14RIK  
 CD99  
 GPR18  
 4933428A15RIK  
 IL1B  
 CCL2  
 GPR98  
 EGLN3  
 C330008K14RIK  
 2210009G21RIK  
 GBP5  
 CD200  
 SLC7A2  
 UPP1  
 PRRY14  
 F10  
 GLRX  
 CLEC7A  
 ABCC5  
 EPST11  
 GYPC  
 MAD  
 EG940327  
 ANTXR1  
 LOC435565  
 ATF3  
 FCGR1  
 BC067047  
 LOC262360  
 CXCL9  
 FGL2  
 ISG20  
 FCGR4  
 LOC10039742  
 IFNB1  
 SLAMF9  
 4930578N16RIK  
 LOC100048556  
 ZFP36  
 STAT2  
 SIGLEC1  
 LRR1  
 CD274  
 EMP1  
 E130207H16RIK  
 CCDC126  
 A530023O14RIK  
 SLEF4  
 LOX  
 IL1RN  
 9030625A04RIK  
 GSTT4  
 TYK1  
 LIPG  
 OTTMUSG00000016644  
 GBP2  
 DLEU2  
 BST1  
 MS444C  
 DTX2  
 PDL7B  
 GBP6  
 PKCFB3  
 FKN2  
 FLNB  
 ZFP36L1  
 CD38  
 BC057170  
 GBP3  
 MOV10  
 ANKRD37  
 A430084P05RIK  
 GBP4  
 BC023892  
 HP  
 SIRPB1  
 APOL9B  
 RP23-357114.1  
 LVEA  
 IFT1  
 MS4A6B  
 IL15  
 FTGES  
 EVL  
 SLAMF7  
 OASL1  
 SCAVENGER RECEPTOR  
 RIN2  
 MARCH1  
 OAS1D  
 MX1  
 CCL7  
 HBP1

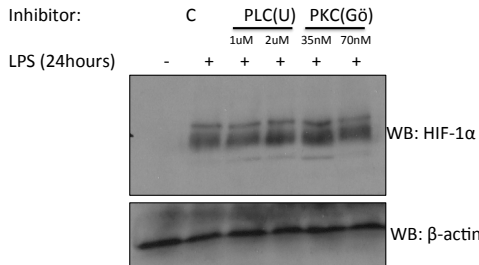


S6. HIF-1 $\alpha$  mRNA in LPS-stimulated BMDMs, pretreated  $\pm$  2DG. S7. LPS-induced, TNF $\alpha$  (left panel) and IL-6 (right panel) in BMDMs incubated in either normoxia (21% oxygen, black bars) or hypoxia (1% oxygen, white bars) for 24 h and then stimulated with LPS for a further 24 h. S8. IL-1 $\beta$  mRNA levels in LPS-stimulated BMDMs pretreated with DMOG (200 $\mu$ M). Error bars  $\pm$  s.e.m, \*  $p < 0.05$ ; \*\*  $p < 0.01$ . S9. RAW-264 cells transfected with the promoter region of human *IL1B* (*IL1B-*) or its variant (*-300 IL1B*). Promoter activity was measured by luciferase assay as relative expression over the unstimulated empty vector control (mean  $\pm$  s.d.). Representative of 3 independent experiments

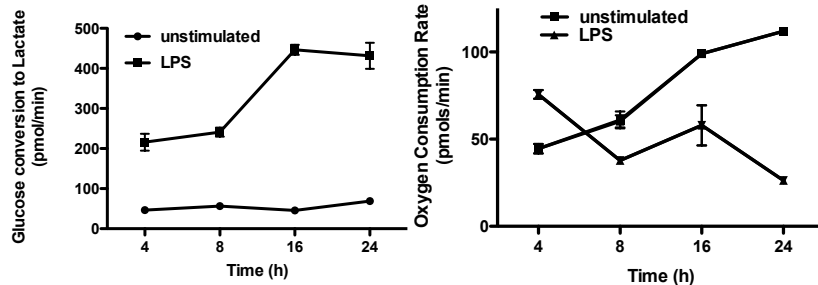
S10



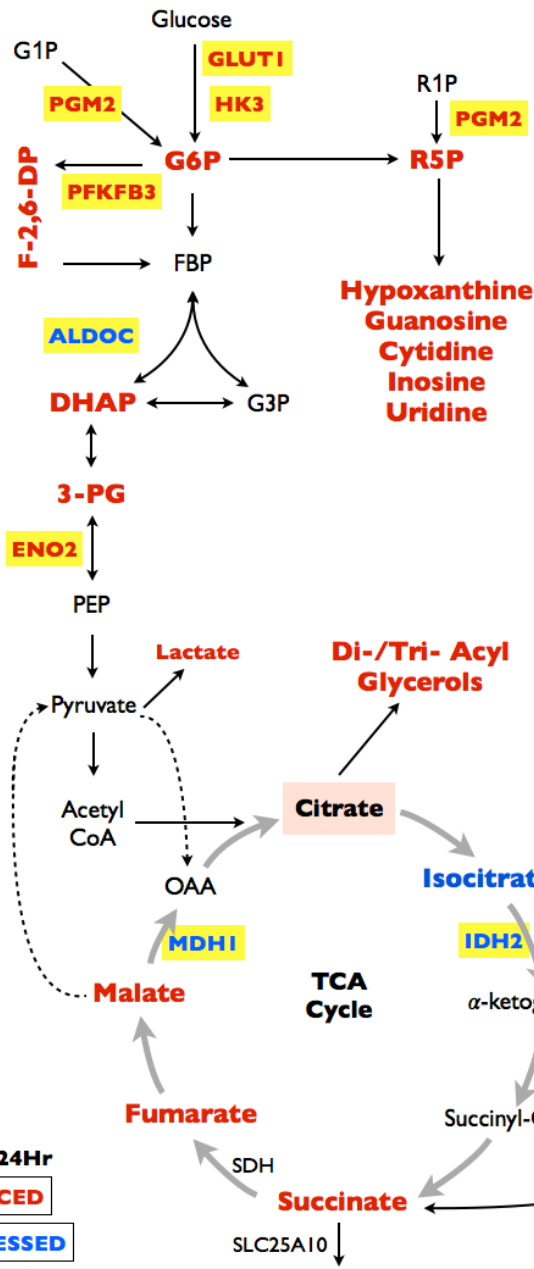
S11



S12

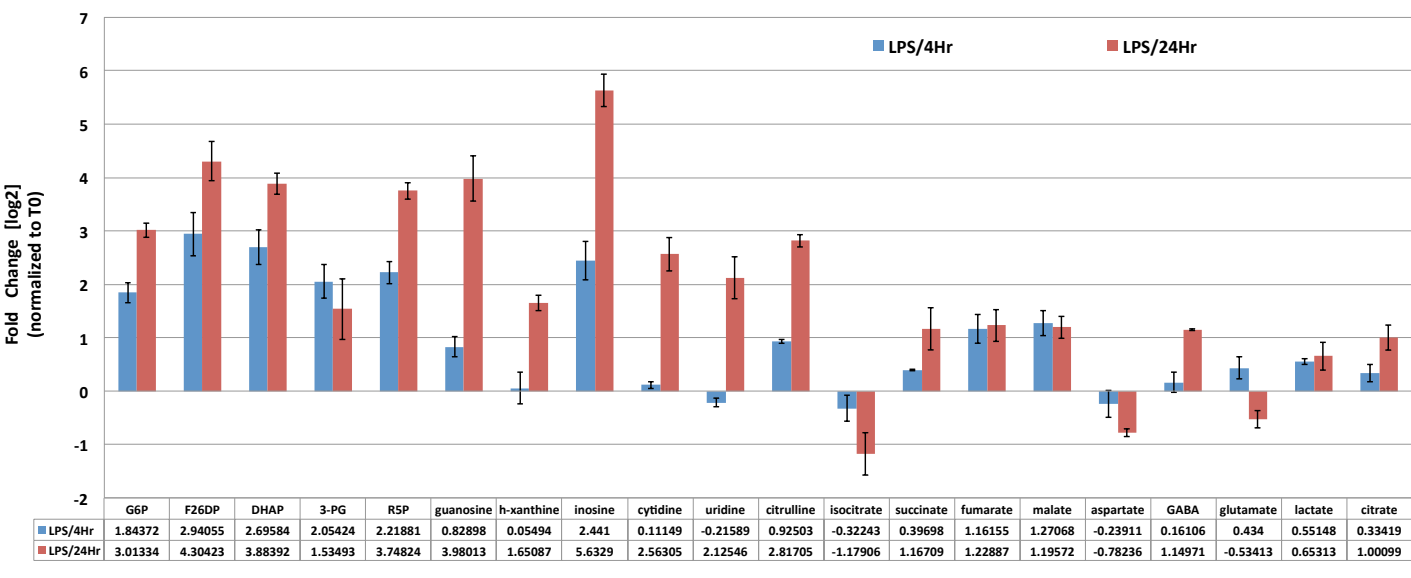


S10. BMDMs stimulated with LPS for 4 and 24 h then stained with CM-H<sub>2</sub>DCFDA and analysed by fluorescence-activated cell sorting (left panel). Quantification of three separate experiments displayed as relative mean fluorescence intensity (MFI) (right panel). HIF-1α expression in BMDMs pretreated with the antioxidant N-acetyl cysteine (NAC) (2.5mM) then LPS for up to 24 h (lower panel). S11. HIF-1α expression in LPS-stimulated BMDMs pretreated with PLC inhibitor (1 or 2μM) and PKC inhibitor (35 or 70nM). S12. BMDMs stimulated with LPS for 24 h were analysed on the Seahorse XF-24 for ECAR and OCR.

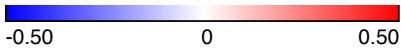


S13. Schematic summarising key metabolites and genes (highlighted in yellow) that were significantly enhanced (red) or inhibited (blue) in BMDMs treated with LPS (100ng/ml) for 4 and 24 h. Statistical analysis was performed on BMDMs from 3 separate experiments. Graph shows 20 metabolites significantly differentially regulated by LPS at 4 and 24 h. Metabolites with p value < 0.05 and fold-change > 10% were deemed to be statistically significant.

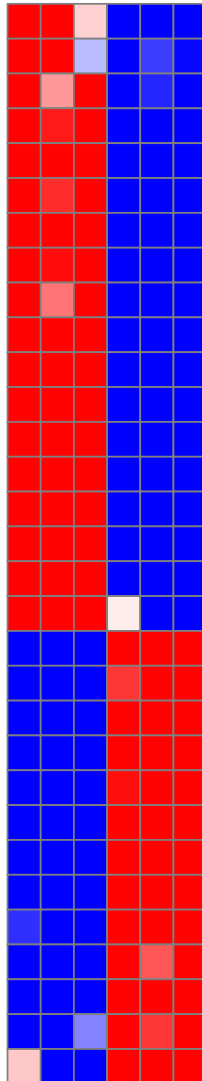
LPS / 24Hr  
**INDUCED**  
**REPRESSED**



### S14



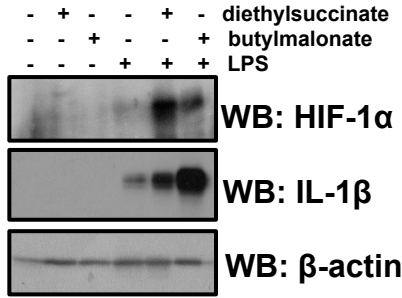
WT1\_LPS\_4h  
WT2\_LPS\_4h  
WT3\_LPS\_4h  
WT1\_LPS\_24h  
WT2\_LPS\_24h  
WT3\_LPS\_24h



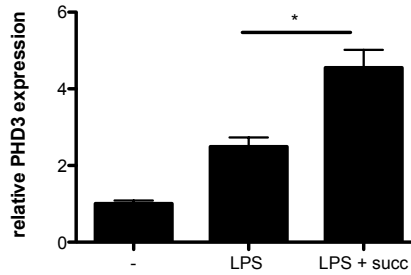
Annotation

SLC11A2  
NUP155  
NUP43  
NUP107  
GOT2  
ALDH1B1  
NUP85  
AAAS  
NUP133  
NUP210  
IDH2  
ALDOC  
SLC39A8  
SLC39A10  
SLC2A6  
NUP205  
PHKA2  
MDH1  
SLC16A10  
SLC6A12  
SLC6A13  
PGM2  
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ENO2  
ACSS2  
SLC39A7  
HK3  
PFKFB3

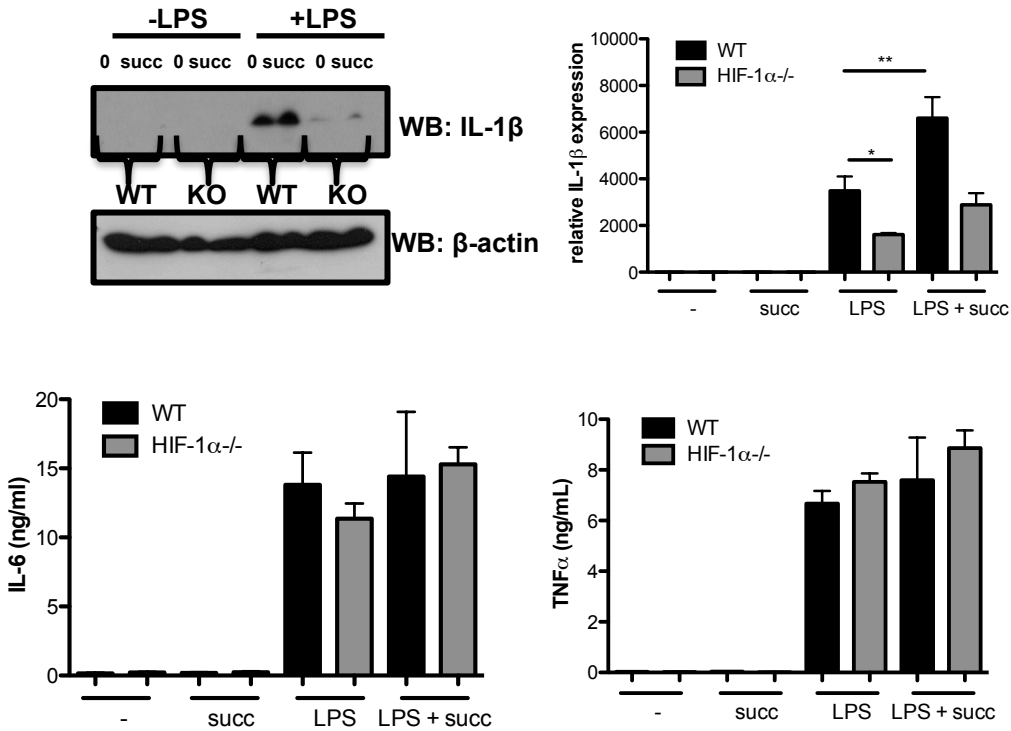
### S15



### S16

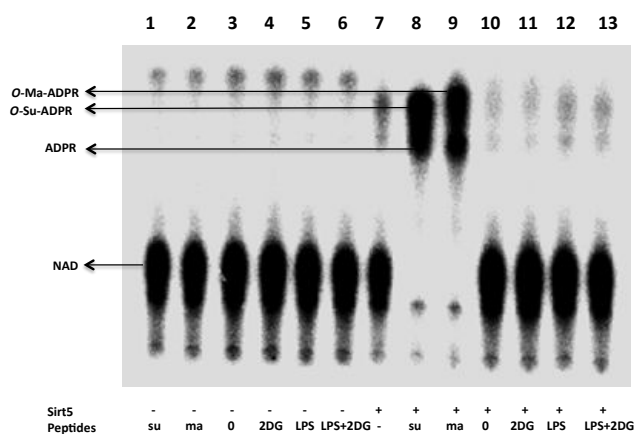


S14. Heat map representing metabolic genes regulated at 4 and 24 h by LPS that were both induced (red) and repressed (blue) in BMDMs. n=3. S15. HIF-1α and IL-1β expression in BMDMs pretreated ± diethylsuccinate (5mM) or ± butylmalonate for 3 h and LPS for 24 h. S16. PHD3 mRNA expression in BMDMs pretreated with diethylsuccinate (succ) (5mM) for 3 h and LPS for 24 h. Error ± s.e.m \* p < 0.05.

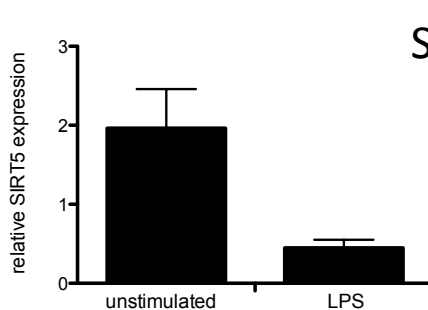


S17. IL-1 $\beta$  protein and mRNA (upper left and right panel) and IL-6 and TNF $\alpha$  (lower left and right panel) expression in WT and HIF-1 $\alpha$ -deficient BMDMs treated  $\pm$  diethyl succinate then LPS stimulated for 24 h. Error bars  $\pm$  s.e.m, \*  $p < 0.05$ ; \*\*  $p < 0.01$ .

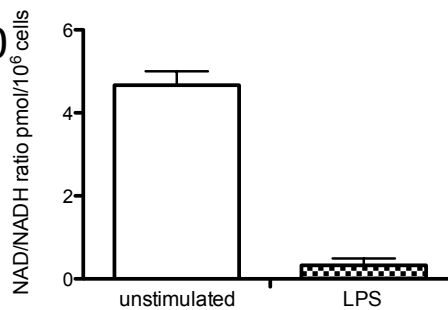
## S18



## S19



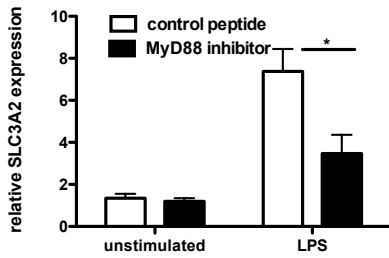
## S20



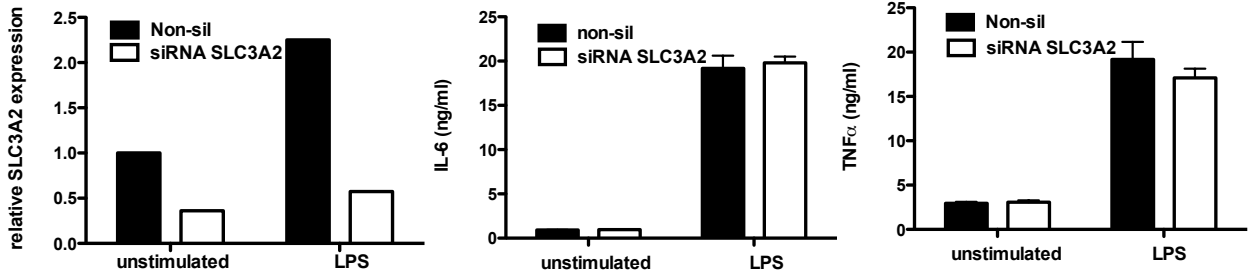
S18. <sup>32</sup>P-NAD assay detecting SIRT5-catalyzed hydrolysis of succinyl and malonyl peptides, which formed <sup>32</sup>P-labeled *O*-Su-ADPR and *O*-Ma-ADPR. Trypsin digested peptides of whole BMDM cell lysates treated with LPS (lane 12) showed higher protein succinylation level compared with control group (lane 10). Synthetic H3K9 succinyl and malonyl peptides were used as positive controls (lane 8 and 9) to indicate the reference positions of *O*-Su-ADPR and *O*-Ma-ADPR. S19. SIRT5 mRNA expression in BMDMs treated with LPS for 4 h. S20. NAD/NADH ratio in BMDMs treated with LPS for 24 h.



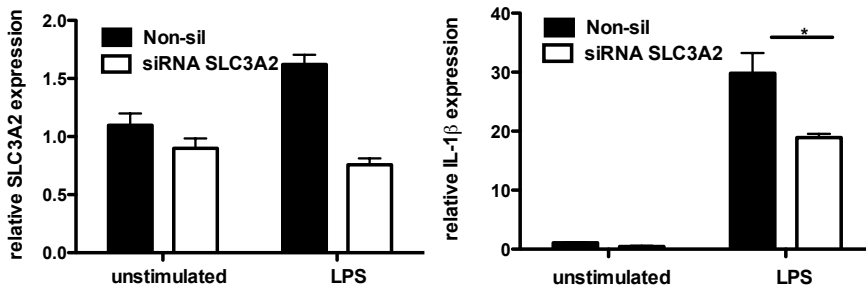
S21



S22

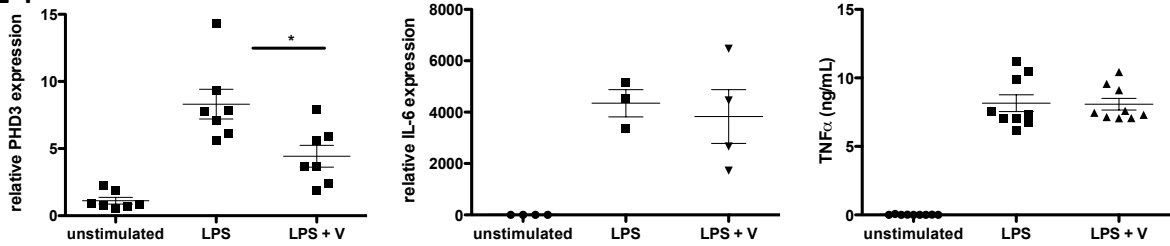


S23

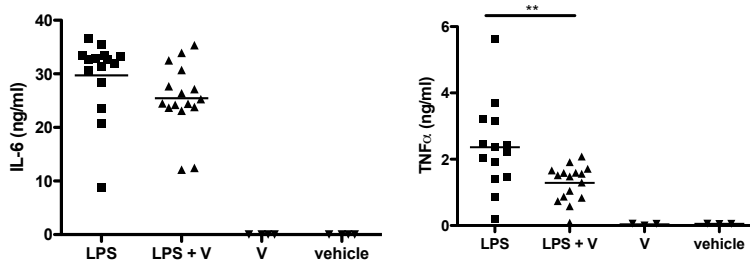


S21. SLC3A2 mRNA in LPS stimulated BMDMs pretreated with control peptide (5 $\mu$ M) or MyD88 inhibitory peptide (5 $\mu$ M) for 5 h. S22. SLC3A2 mRNA, IL-6 and TNF $\alpha$  protein in human PBMCs with SLC3A2 expression knocked down using 100nM siRNA compared to 100nM siRNA of a non-silencing control. Data shown is representative of 3 separate experiments Error bars,  $\pm$ s.d. S23. SLC3A2 and IL-1 $\beta$  mRNA expression in RAW-264 cells transfected with either 100nM siRNA or 100nM siRNA of a non-silencing control. n=3. Error bars  $\pm$  s.e.m, \* p < 0.05.

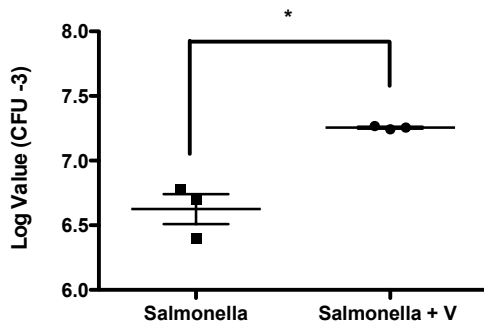
S24



S25



S26



S24. PHD3 mRNA (n=7), TNF $\alpha$  protein (n=9) and IL-6 mRNA (n=4) in serum-deprived LPS-stimulated BMDMs pretreated  $\pm$  vigabatrin (500 $\mu$ M) for 30 min. S25. Mice i.p. injected  $\pm$  vigabatrin (400mg/kg) or PBS for 1.5 h, then 15 mg/kg LPS or PBS for 1.5 h. Serum levels of IL-6 and TNF $\alpha$ . LPS n=16; LPS+vigabatrin (LPS + V) n=14; vigabatrin (V) n=3; vehicle n=3. S26. Mice i.p. injected mice  $\pm$  vigabatrin (400mg/kg) or PBS for 1.5 h then infected with  $1 \times 10^6$  *Salmonella* Typhimurium UK1 i.p. for 2 h. Spleens were harvested, homogenised in PBS and following serial dilution plated onto agar plates and left at 37 $^{\circ}$ C overnight, bacterial load was assessed by colony forming units (CFU). Error bars  $\pm$  s.e.m, \* p < 0.05; \*\* p < 0.01.