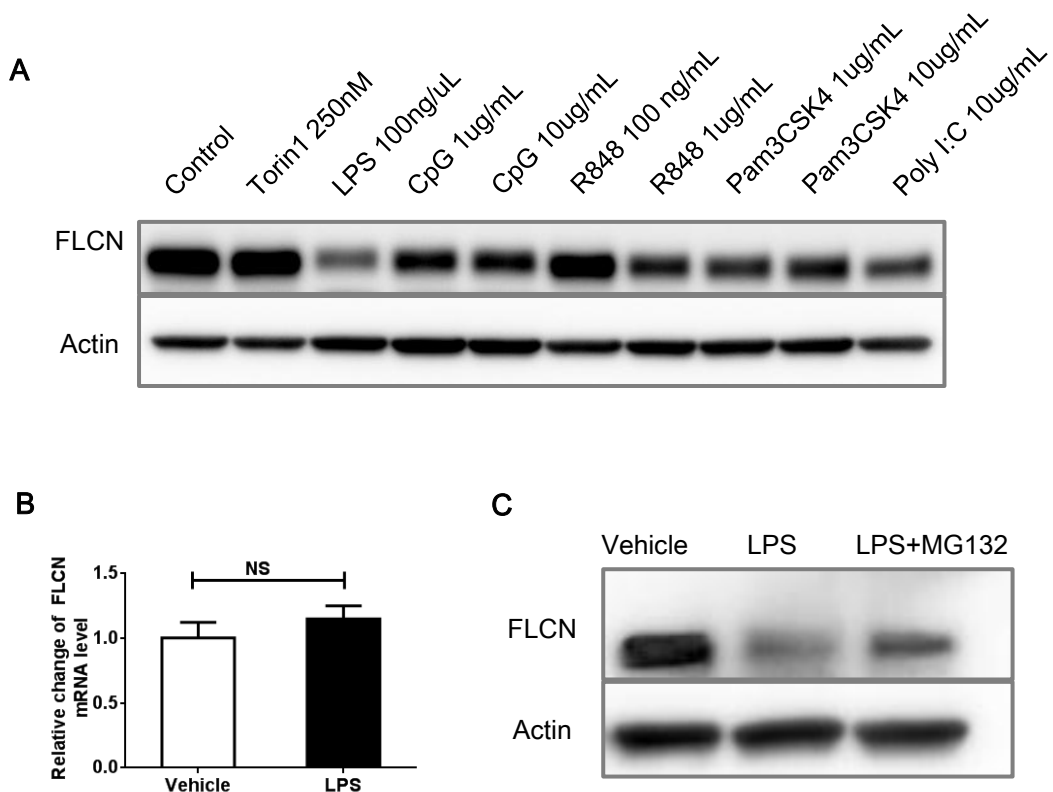
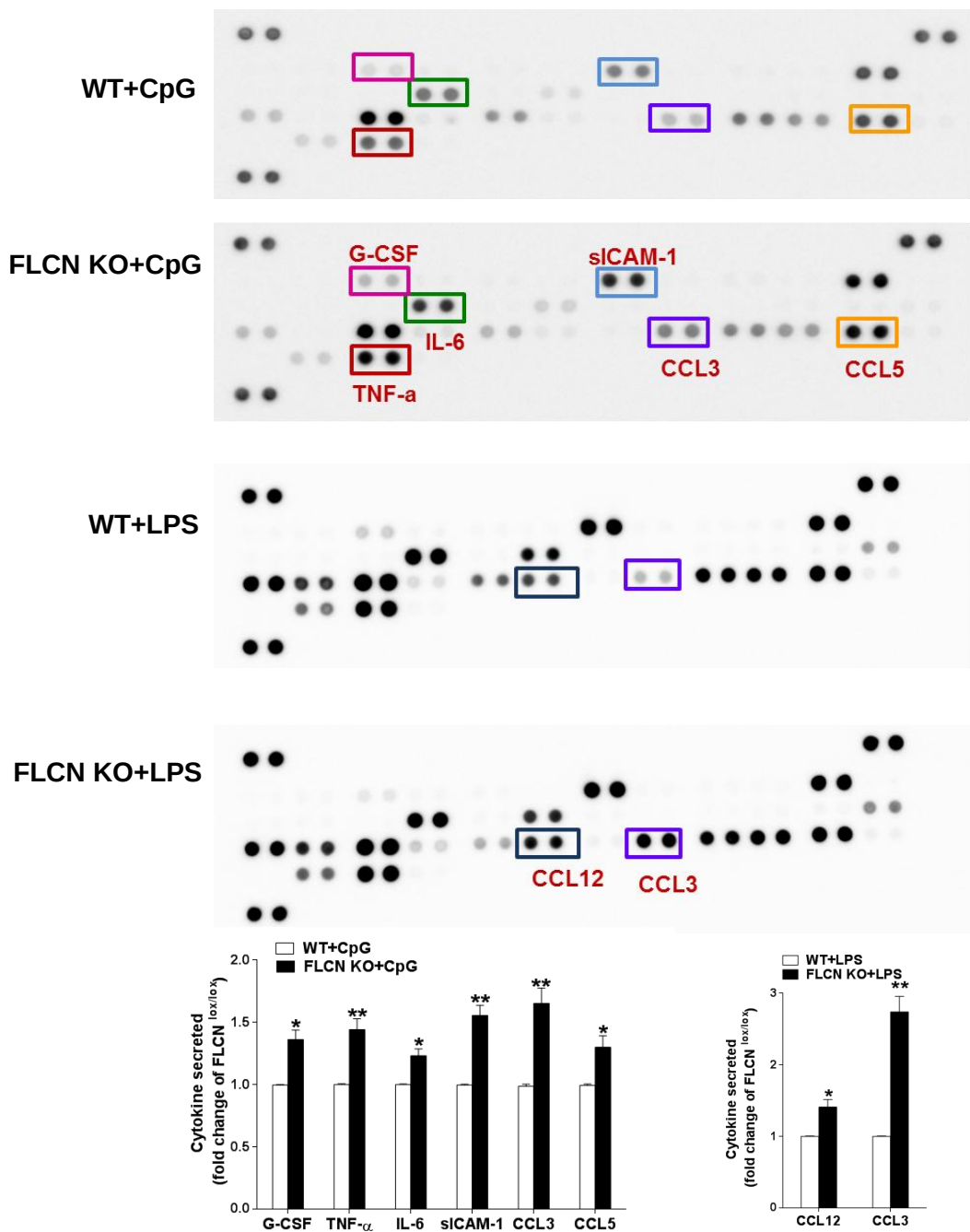
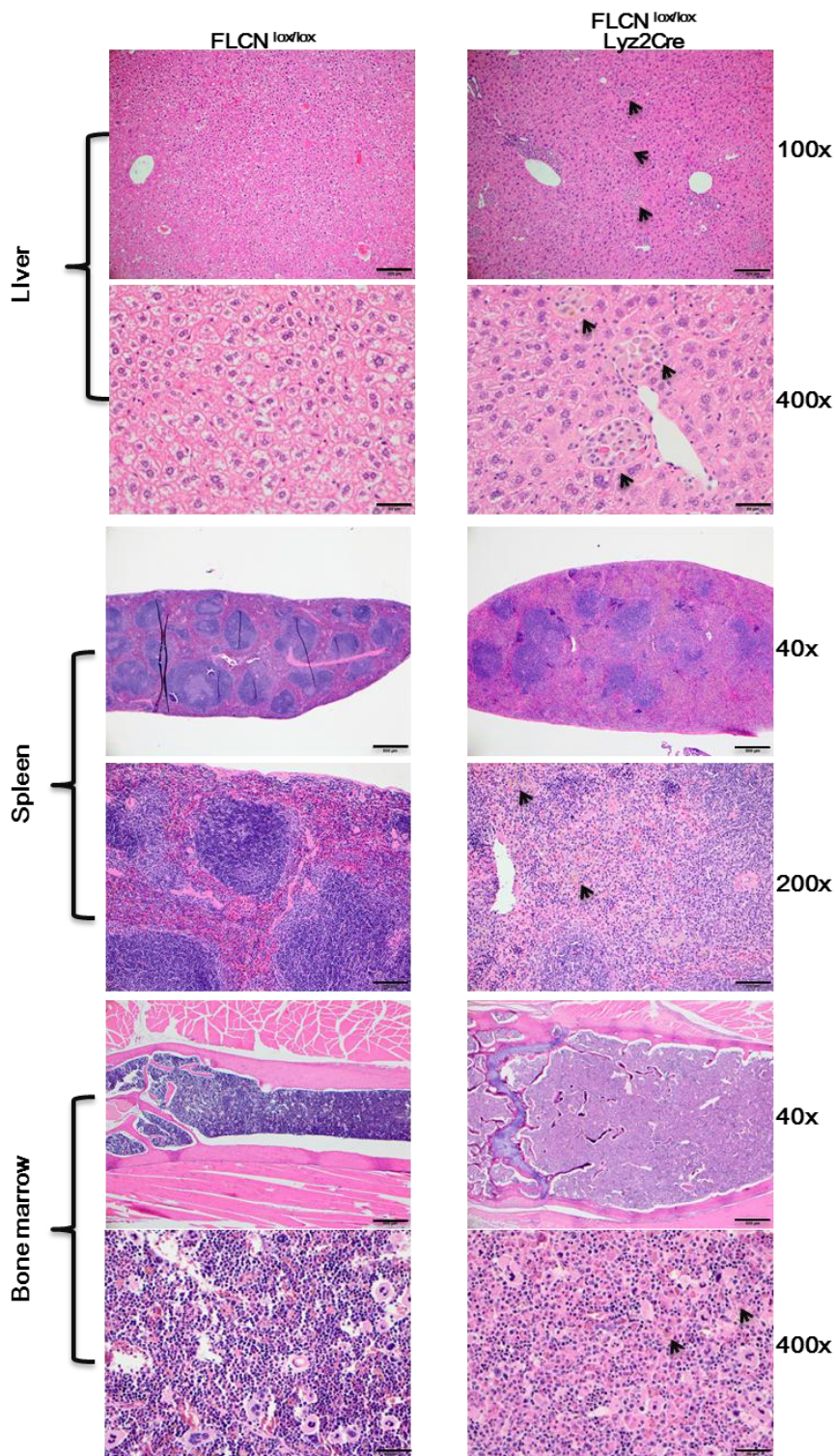




Supplementary Figure 1. (A) FLCN expression was determined in BMDMs exposed to different TLR agonists for 24h. LPS (TLR 4 agonist), CpG DNA (TLR9 agonist), R848 (TLR7/8 agonist), Pam3CSK4 (TLR1/2 agonist), Poly I:C (TLR3 agonist). (B) Relative mRNA expression of FLCN in BMDMs treated with Vehicle or LPS for 24 h. NS: no significance. (C) FLCN expression was determined in BMDMs exposed Vehicle, LPS or LPS+MG132 (the proteasome inhibitor, 250 nM) for 24h.



Supplementary Figure 2. Cytokine array blots for WT and FLCN KO BMDMs that were stimulated with CpG (10 ug/ml) or LPS (100 ng/ml) for 24 h. Cytokine and chemokine levels of the supernatant were detected using the Mouse Cytokine Array Assay kit (R&D Systems) following manufacturer's protocol. Bar graph: Quantification of cytokine and chemokine spots on each blot were performed using ImageJ. (n=3). G-CSF: granulocyte-colony stimulating factor, TNF- α : tumor necrosis factor- α , IL-6: interleukin-6, sICAM-1: soluble intercellular adhesion molecule-1 CCL: chemokine [C-C motif] ligand.



Supplementary Figure 3. Hematoxylin and eosin staining of liver, spleen and bone marrow from $FLCN^{lox/lox}$ and $FLCN^{lox/lox}$ $Lyz2^{Cre}$ mice at 12 months. Haemophagocytosis was indicated by black arrow.

Supplemental Table 1

Name	Primer sequences
mu 36B4 f	GAGACTGAGTACACCTTCCCAC
mu 36B4 r	ATGCAGATGGATCAGCCAGG
mu Hpvt f	GTTAAGCAGTACAGCCCCAAA
mu Hpvt r	AGGGCATATCCAACAACAACTT
mu Gapdh f	AGGTCGGTGTGAACGGATTTG
mu Gapdh r	TGTAGACCATGTAGTTGAGGTCA
mu Arg1 f	AGACCACAGTCTGGCAGTTG
mu Arg1 r	CCACCCAAATGACACATAGG
mu Clec10a f	CTCTGGAGAGCACAGTGGAG
mu Clec10a r	ACTTCCGAGCCGTTGTTCT
mu Flcn f	CTATCCCTGCCCATGTTCTG
mu Flcn r	GTGGAGGTTTGAGCGAGT
mu Tfe3 f	GCAGGCGATTCAACATTAACG
mu Tfe3 r	GCTGTTCTTCTGTAATTTGCG
mu Tfeb f	CGAGAGCTAACAGATGCTGAG
mu Tfeb r	GCATTCCCAGCTCCTTGAT
mu Tfec f	GGCTGTTGCTTACAACCTGACT
mu Tfec r	AGCGGCACTAAAGGATAAATCTG
mu Gpnmb f	CCTTCAATGGGTCTGGCAC
mu Gpnmb r	ACACCATTCACTGCTCTCATAG
mu Lamp1 f	TGGAGAACAAGAACAGAGCC
mu Lamp1 r	TTGGAGATGCTGAATGTGGG
mu Ctsz f	GGGCAATGACCTTCCGGTG
mu Ctsz r	AACTTGTACAGTCTTGGTCC
mu Ctsd f	GCTTCCGGTCTTTGACAACCT
mu Ctsd r	CACCAAGCATTAGTTCTCCTCC
mu Hexa f	TGGCCCCAGTACATCCAAAC
mu Hexa r	GGTTACGGTAGCGTCGAAAGG
mu Mcoln1 f	CAGCATCGAATCCTGGACCG
mu Mcoln1 r	GCTCCCCAACTTGATGACATTG
mu Tpp1 f	GAGTCTCACTTTTGCGCTGAA
mu Tpp1 r	CTCCAGGGTTAGGTACTTTCCA
mu Clcn7 f	CGCCAGTCTCATTCTGCACT
mu Clcn7 r	GCTTCTCGTTGTGTGGAATCT
mu RagA f	CACTCCCACGTCCGATTCTTG
mu RagA r	GCGGCTCTCTACGTCAAACA
mu RagB f	CTAGCCAGCGTGACAACATCT
mu RagB r	GCCTCAAGGCATGACTGATAGT
mu RagC f	AGATGTCACCCAATGAGACTCT
mu RagC r	AGTCGTCCTGTGCATCAATGA
mu RagD f	CTGTTTGACGTGGTCAGTAAGAT
mu RagD r	GTTGAGTCCTTGTCATACGGG

mu Rictor f
mu Rictor r
mu Raptor f
mu Raptor r

ACAGTTGGAAAAGTGGCACAA
GCGACGAACGTAGTTATCACCA
TTTGTCTACGACTGTTCCAATGC
GCTACCTCTAGTTCCTGCTCC