Supplementary Table Oligonucleotide primers used in PCR-based experiments

Gene name	Amplified region	Experiment	Forward primer (5' to 3')	Reverse primer (5' to 3')
Mapk14	Downstream loxP	Genotyping	atgagatgcagtaccctggagaccagaag	agccagggctatacagagaaaaaccctgtg
Cre	ORF	Genotyping	ggtcgatgcaacgagtgatgaggt	cagcattgctgtcacttggtcgtg
Mapk14	Exon 2	KO efficiency	ggtcagcagcctcgatgcac	gactgcccctccaaccgttc
Mapk14	Exon 12	KO efficiency	gccctccctcacttcaggag	tgtgctcggcactggagacc
Dusp1	Promoter	ChIP	gtctttgcttttggctttgg	cgcggttttatgtagcctct
Il10	Promoter	ChIP	cagaagttcattccgaccagt	ccttcctggcaaaggttttt
Nfkbia	Promoter	ChIP	aaagttccctgtgcatgacc	ggaatttccaagccagtcag
Areg	cDNA	qPCR	atgggactgtgcacgccatt	atttccggtgtggcttggcaat
Bcl2a1	cDNA	qPCR	tgtggcagaattcataatgaataacaca	aaacttctttatgaagccatcttccc
Bcl3	cDNA	qPCR	ttactctaccccgacgatgg	ggtgagtaggcaggttcagc
Birc2	cDNA	qPCR	ggaaattgactccacgttatatgaaaact	gctcttccaatgacaagcctga
Birc3	cDNA	qPCR	ggaaattgaccctgcgttatacaga	tctcggtccatacacactttacacatt
Ccl2	cDNA	qPCR	gccagctctctcttcctcca	cccagaagcatgacagggac
Ccl3	cDNA	qPCR	ccaagtcttctcagcgccat	tccggctgtaggagaagcag
Ccl4	cDNA	qPCR	gacttggagttgaactgagcagc	aggcctctcctgaagtggc
Ccl5	cDNA	qPCR	aatcccctactcccactcgg	ttcttgggtttgctgtgcag
Ccrl2	cDNA	qPCR	tgctcttcctctgctggttt	gaagctctgccttctcctca
Cd38	cDNA	qPCR	ggaaagatgttcaccctgga	ccacctgagatcatcagcaa
Cflar	cDNA	qPCR	tttgtcatgcgactgggtaa	gggtcacagaaattggtggc
Ch25h	cDNA	qPCR	ccacgacatgcatcactctc	gcattttgtcccagtgtgtg
Cish	cDNA	qPCR	cccagaggaagtgacagagg	ggtctagcaccttcggttca
Csf2	cDNA	qPCR	ggccttggaagcatgtagag	gcatgtcatccaggaggttc
Cxcl1	cDNA	qPCR	gccaatgagctgcgctgt	ccttcaagctctggatgttcttg
Cxcl10	cDNA	qPCR	gaatccggaatctaagaccatcaa	gtgcgtggcttcactccagt
Cxcl2	cDNA	qPCR	atccagagcttgagtgtgacgc	aaggcaaacttttgaccgcc
Dusp1	cDNA	qPCR	ccatctgccttgcttacctc	aagctgaagttcggggagat
Edn1	cDNA	qPCR	aaggcatcttttcgtgttgc	ttgtgcgtcaacttctggtc
G1p2	cDNA	qPCR	accctttccagtctgggtct	tcgctgcagttctgtaccac
Gadd45b	cDNA	qPCR	tatttgacagccccctcatc	cccagaaggtatcacgggta
Gpr109a	cDNA	qPCR	atgaaaacatcgccaaggtc	ccaggagtccgaacacaaat
Hdc	cDNA	qPCR	agcacaagctgtcgtccttt	gcgttgtcttcctcgtgttc
Icam1	cDNA	qPCR	tggccctgcaatggctt	gcaggaaggcttctctgggat
Icosl	cDNA	qPCR	ctccagggatcaatgtggac	atggagtccagggacagatg
Ifnb1	cDNA	qPCR	agctccaagaaaggacgaacat	gccctgtaggtgaggttgatct
Il10	cDNA	qPCR	gaagctgaagaccctcagga	ttttcacaggggagaaatcg
Il12a	cDNA	qPCR	cagaaacctcctgtgggaga	ggagctcagatagcccatca
Il12b	cDNA	qPCR	atccagcgcaagaaagaaaa	ggaacgcacctttctggtta
Il15	cDNA	qPCR	atcctgctgtgtttggaagg	gtgctttgaagagccagagg
Il1a	cDNA	qPCR	tccagggcagagagggagt	ggaactttggccatcttgattt
Il1b	cDNA	qPCR	gtggctgtggagaagctgtg	gaaggtccacgggaaagacac
Il6	cDNA	qPCR	ccagaaaccgctatgaagttcc	ttgtcaccagcatcagtccc
Krt14	cDNA	qPCR	ggcaagagtgagatttctgagc	tttcatgctgagctgggact
Mapk11	cDNA	qPCR	taccatgaccctgacgatga	tccttggcctcaacactttc
Mapk12	cDNA	qPCR	cccctcctgagtttgttcag	agggaggccttccatgtagt
Mapk13	cDNA	qPCR	gtctgttggttgcatcatgg	tccttgcccttgaagagtgt
Mapk14	cDNA	qPCR	gcatcgtgtggcagttaaga	gtccttttggcgtgaatgat
Mmp13	cDNA	qPCR	tttattgttgctgcccatga	ggtccttggagtgatccaga
Nfkbia	cDNA	qPCR	ctcacggaggacggagactc	ctcttcgtggatgattgcca
Nos2	cDNA	qPCR	caagcaccttggaagaggag	ccaaatgtgcttgtcaccac
Pde4b	cDNA	qPCR	gaggggaatggagattagcc	tgggatttttccacagaagc
Pml	cDNA	qPCR	ggaaacagaggagcgagttg	cagattctcggtgtccgaat
Ppia	cDNA	qPCR	atggtcaaccccaccgtgt	ttcttgctgtctttggaactttgtc
Ptgs2	cDNA	qPCR	cccccacagtcaaagacact	ggttctcagggatgtgagga
Sdc4	cDNA	qPCR	atctggatgacacggaggag	gcattctcagggatgtggtt
Serpina3g	cDNA	qPCR	ccaaatggtgagggtgcttct	gcatagcggatcaccaaaaca
Serpinb2	cDNA	qPCR	tttctttctgaggtgttccatcaa	ccagctgccacagtgcc
Serpine1	cDNA	qPCR	gtctttccgaccaagagcag	caaaggctgtggaggaagac
Sod2	cDNA	qPCR	ggccaagggagatgttacaa	aatatgtcccccaccattga
Tnf	cDNA	qPCR	acagaaagcatgatccgcg	gccccccatcttttggg
Tnfaip3	cDNA	qPCR	cagttccgagagatcatccacaaag	catgaggcagtttccatcacca
Tnfsf10	cDNA	qPCR	ggatatggcctggctgtaga	gttccagctgcctttctgtc
Usp18	cDNA	qPCR	gacgcaaagcctctgaaaac	cacatgtcggagcttgctaa
Vcam1	cDNA	qPCR	aacggtactttggatactgtttgca	gcaagtgagggccatgga
Zc3h12a	cDNA	qPCR	caacgctctcctctcacctc	ggaaggcctctggctacttt

SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1 p38α$^{\Delta M}$ and p38α$^{\Delta K}$ mice exhibit efficient, cell type-specific *Mapk14* ablation. (**a**) WT and cell type-specific p38α knockout mice used in the study. (**b**) Genomic DNA from WT and p38α$^{\Delta M}$ BMDMs was analyzed by qPCR with primer pairs specific to exon 2 and exon 12 of the p38α gene *Mapk14*. Relative copy numbers of exon 2, which is flanked by loxP sites, versus exon 12 are shown as percent dosage. (**c**) Genomic DNA from the liver and epidermis of WT and p38α$^{\Delta K}$ mice were analyzed as in (**b**). Data are representative of analysis of three independently generated BMDM preparations (**b**) or five litters (**c**).

Supplementary Figure 2 p38α deletion does not affect the expression of other p38 isoforms. Expression of p38 isoforms in BMDMs, PEMs, keratinocytes (Kc), MEFs, B16 (mouse melanoma) cells, and splenic T cells (TC) was analyzed by qPCR. p38α, p38β, p38γ, and p38δ are encoded by *Mapk14*, *Mapk11*, *Mapk12*, and *Mapk13*, respectively. Data are from analysis of the same set of cDNA samples in duplicate.

Supplementary Figure 3 Cre recombinase does not perturb gene expression in macrophages and keratinocytes. (**a**) Gene expression in WT and *LysMCre* BMDMs (*n*=2) after 4 h of LPS treatment was analyzed by qPCR. (**b**) The shaved back skin of WT and *K14Cre* mice (one animal of each genotype) was irradiated with UVB (160 mJ/cm^2). After 96 h, gene expression in the epidermal tissues in two separate skin areas was analyzed by qPCR.

Supplementary Figure 4 Myeloid p38α signaling is essential for induction of keratotic lesions in SDS-treated skin. The shaved back skin of the indicated mice was treated daily with 5% SDS, and photographed on day 7. Data are representative of five independent experiments involving a group of three to five mice.

Supplementary Figure 5 UVB-induced skin injury depends on epithelial p38α signaling. The shaved back skin of the indicated mice was irradiated with UVB (160 mJ/cm^2), and photographed on day 4. Arrowheads (red) indicate 'sunburn' lesions. Data are representative of six independent experiments involving a group of three to five mice.

Supplementary Figure 6 $p38\alpha^{\Delta M}$ PEMs are defective in LPS induction of the same set of p38α target genes identified from experiments using BMDMs. Expression of genes in WT and $p38\alpha^{\Delta M}$ PEMs (*n*=3) after 0, 2, and 4 h of LPS treatment was analyzed by qPCR.

Supplementary Figure 7 $p38\alpha^{\Delta M}$ neutrophils do not exhibit impaired migration toward KC and MIP-2. (**a**) Whole cell lysates from WT and $p38\alpha^{\Delta M}$ neutrophils (isolated from one animal of each genotype) were analyzed by immunoblotting with anti-p38α and anti-actin. (**b**) Migration of WT and $p38\alpha^{\Delta M}$ neutrophils was analyzed by a transwell assay (*n*=2) without or with the chemokines indicated.

Supplementary Figure 8 Removal of p38α does not impair NF-κB activation. (**a, b**) Cytoplasmic (Cyto) and nuclear (Nuc) extracts from BMDMs treated with LPS (**a**), and

keratinocytes irradiated with UVB (**b**) were prepared at the indicated time points and analyzed by immunoblotting with antibodies against the proteins indicated on the left. Data are representative of two independent experiments.

Supplementary Figure 9 Removal of p38α in macrophages does not lead to a change in ROS production. BMDMs were left untreated or treated with LPS for 30 min, and then incubated with dichlorodihydrofluorescein diacetate for additional 30 min. ROS production (fluorescence) was analyzed by confocal microscopy. Fluorescence and bright field images are shown in pair. The numbers represent relative fluorescence intensities. Data are representative of at least three independent images.

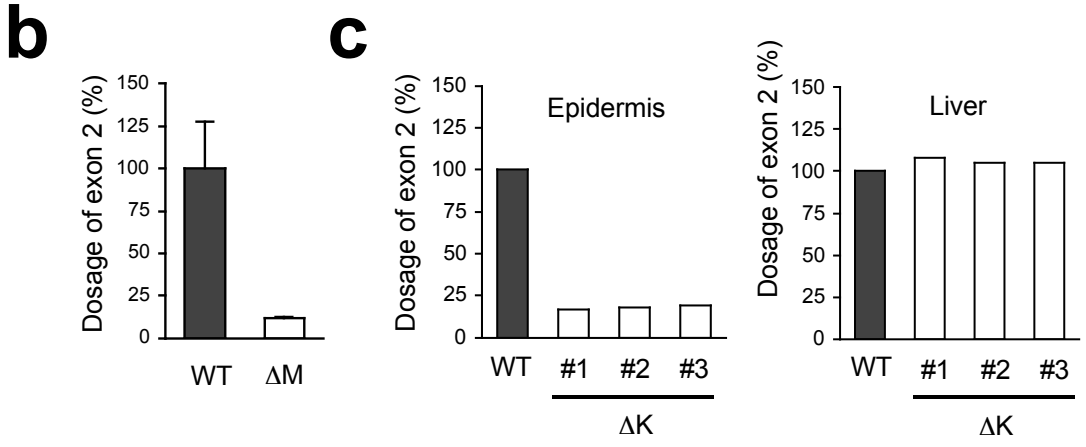
Supplementary Figure 10 Stability of mRNA in WT and $p38\alpha^{\Delta M}$ BMDMs was analyzed by qPCR. Cells were treated with LPS for 2 h and then incubated with actinomycin D (actD) for the indicated durations before RNA isolation. Data are from one experiment.

Supplementary Figure 11 p38α signaling plays cell type-specific roles in regulation of inflammation. The thickness of lines indicates the relative strength of the signaling events that they denote. (**a**) SDS-induced chronic skin inflammation. (**b**) UVB or TPA-induced acute skin inflammation.

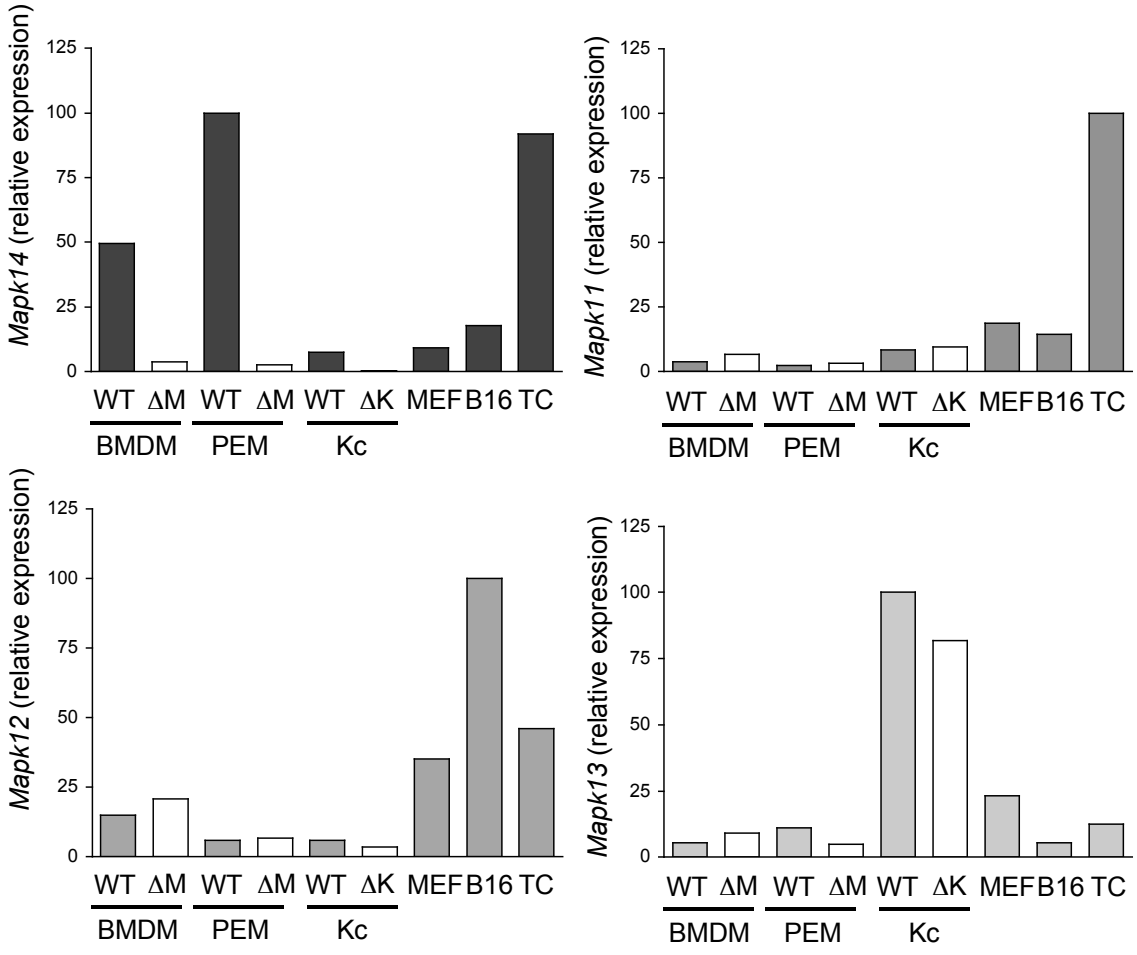
Supplementary Figure 1

a

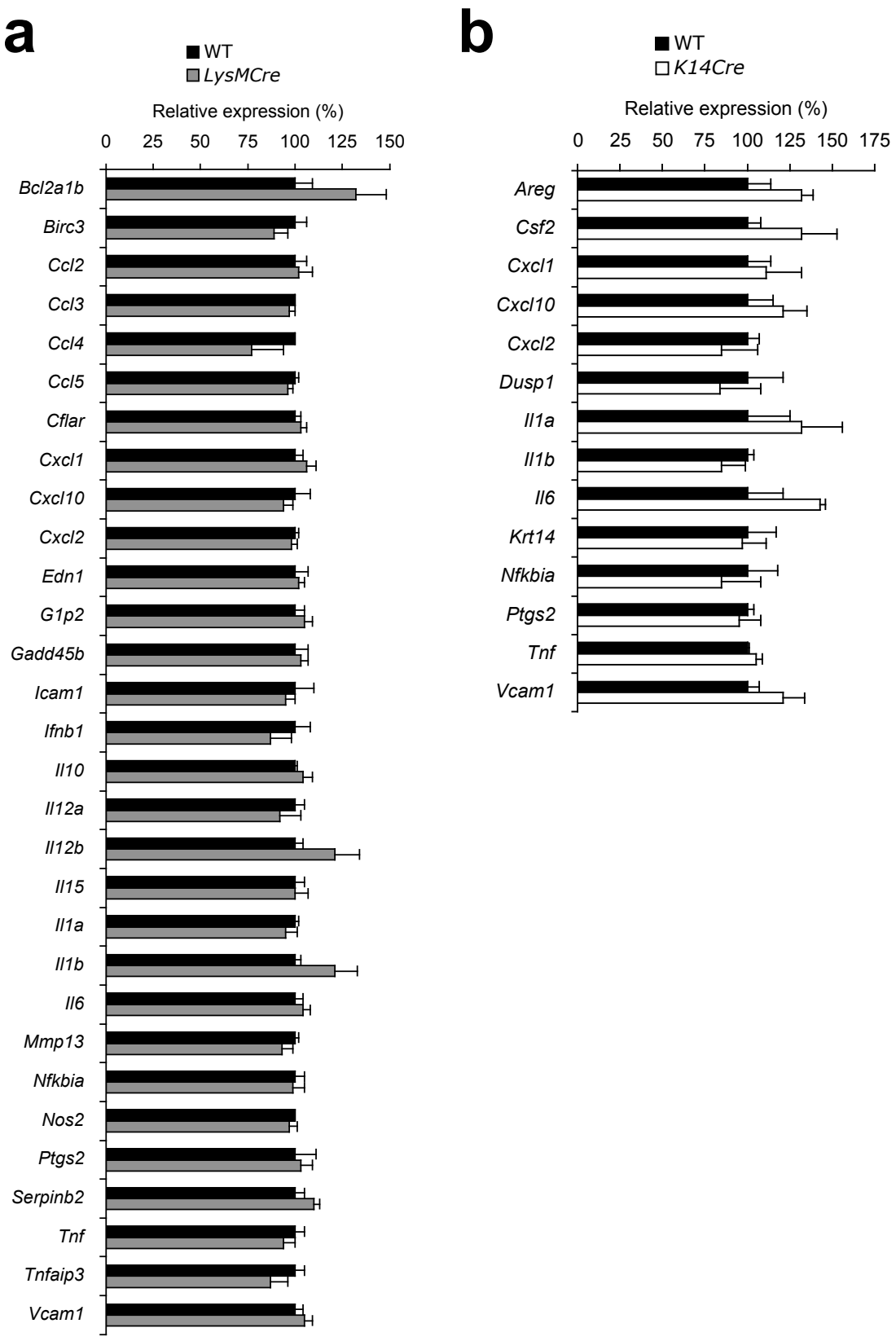
WT	*Mapk14$^{fl/fl}$*	p38α wild type
p38α$^{\Delta M}$	*Mapk14$^{fl/fl}$;LysMCre*	Myeloid-specific knockout
p38α$^{\Delta K}$	*Mapk14$^{fl/fl}$;K14Cre*	Keratinocyte-specific knockout



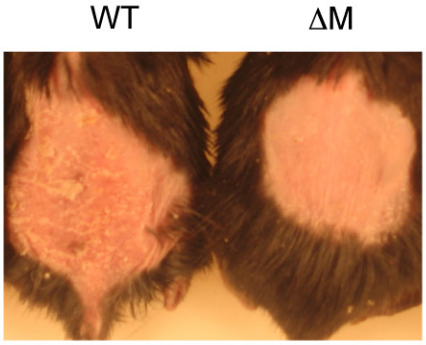
Supplementary Figure 2



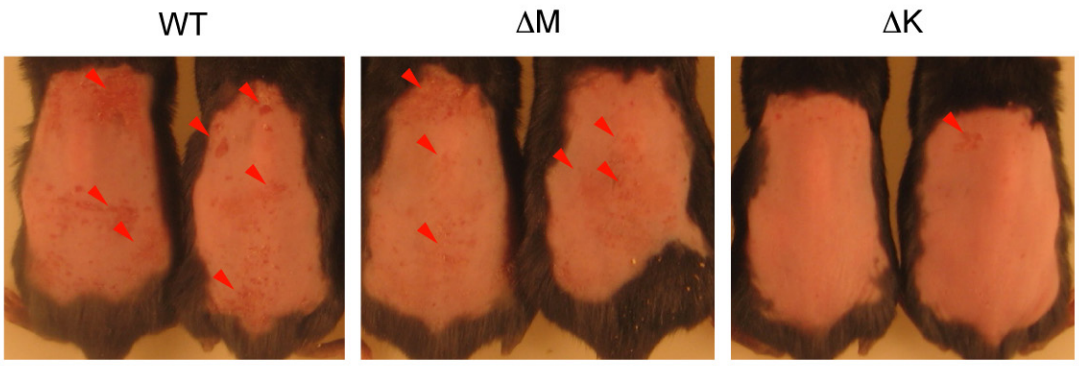
Supplementary Figure 3



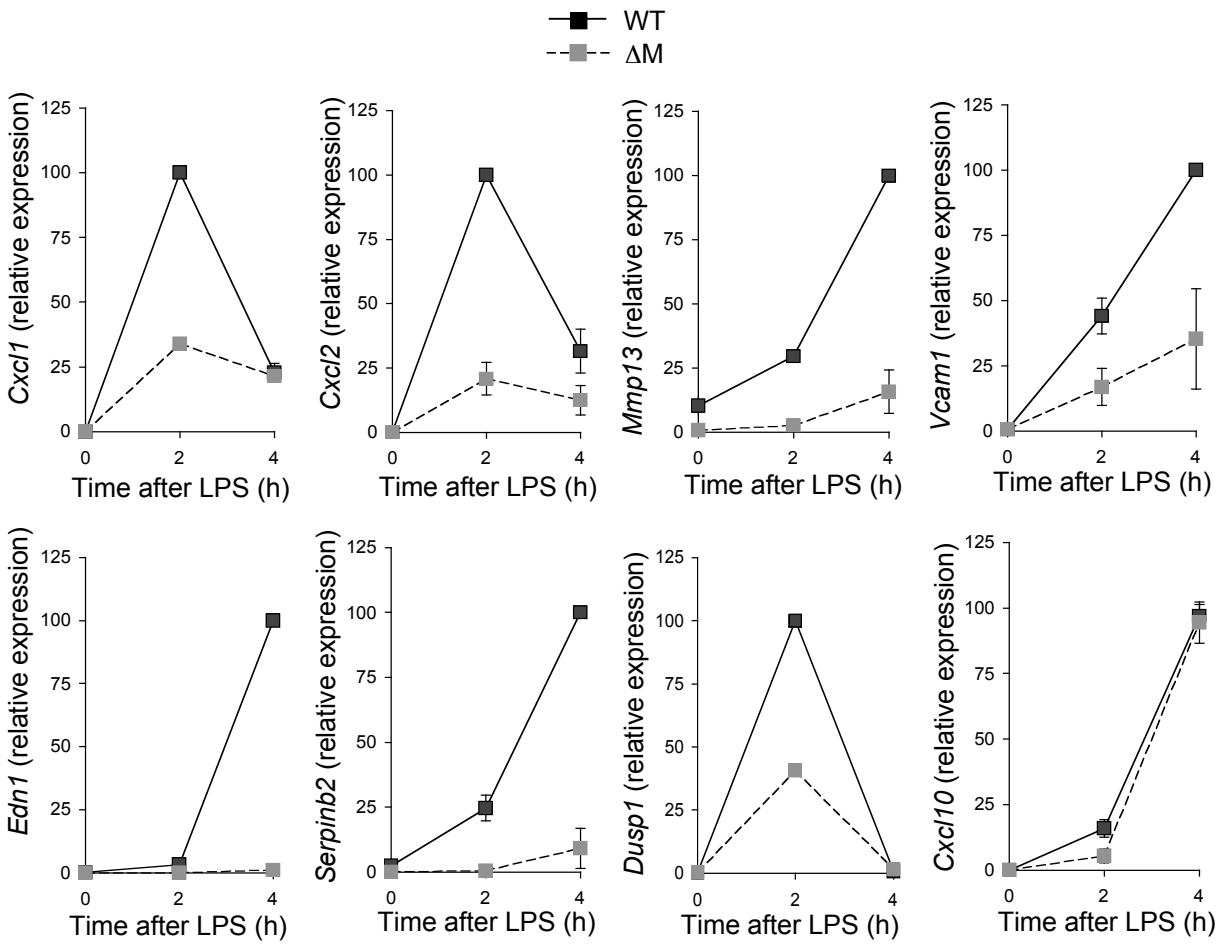
Supplementary Figure 4



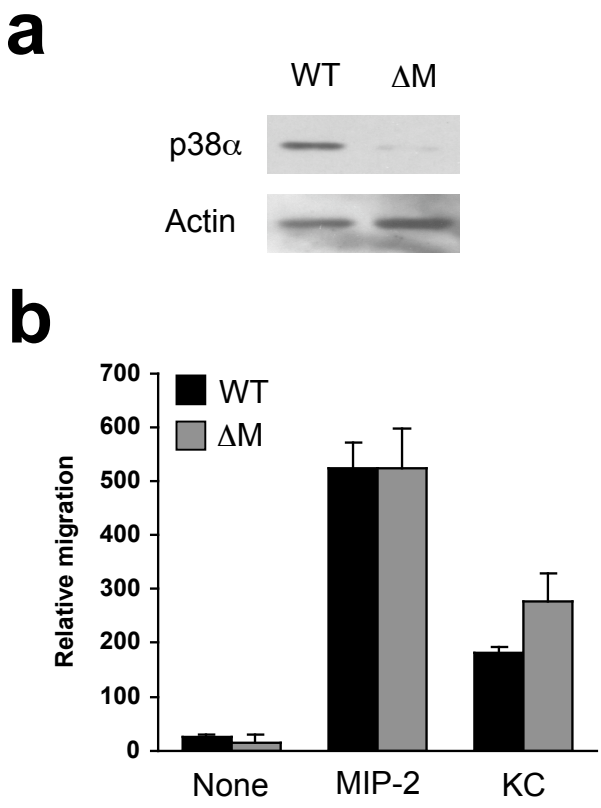
Supplementary Figure 5



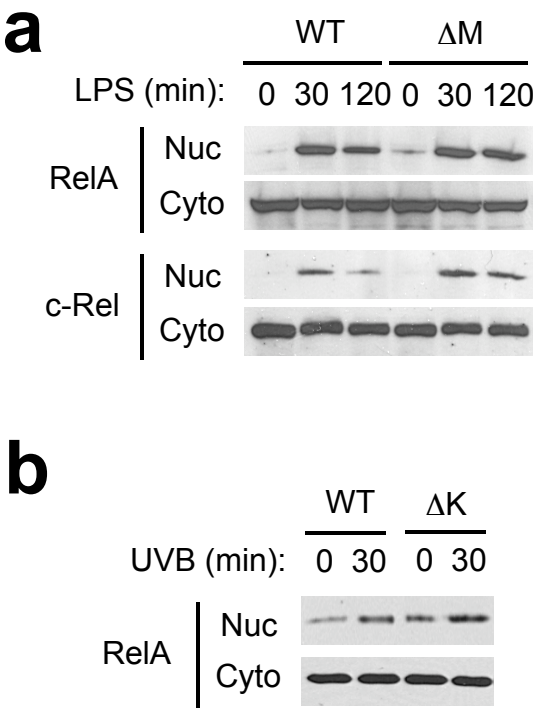
Supplementary Figure 6



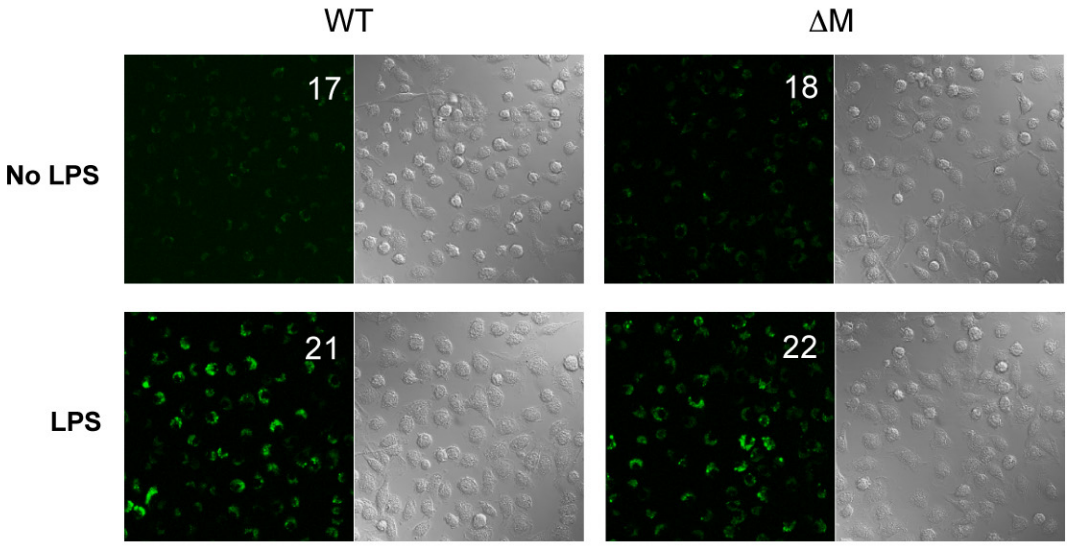
Supplementary Figure 7



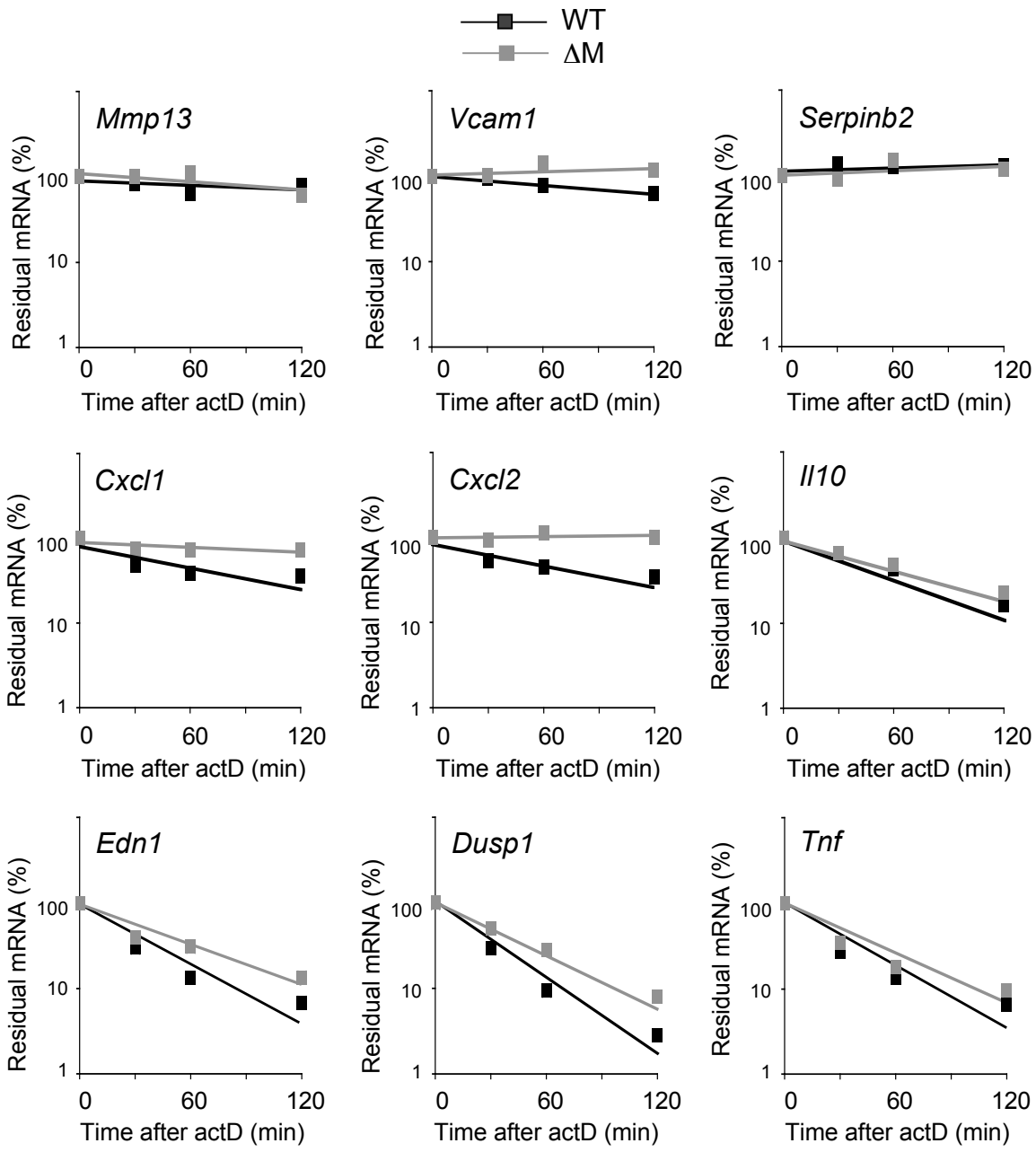
Supplementary Figure 8



Supplementary Figure 9



Supplementary Figure 10



Supplementary Figure 11