Figure S1

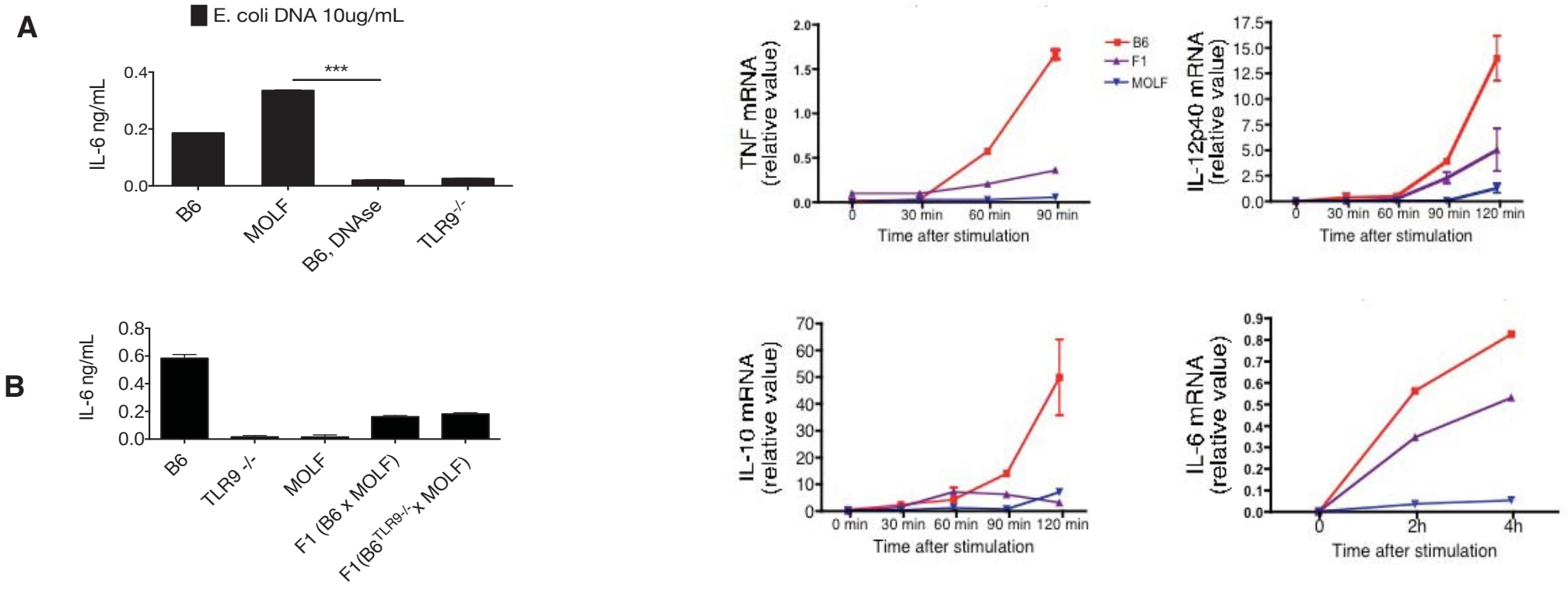

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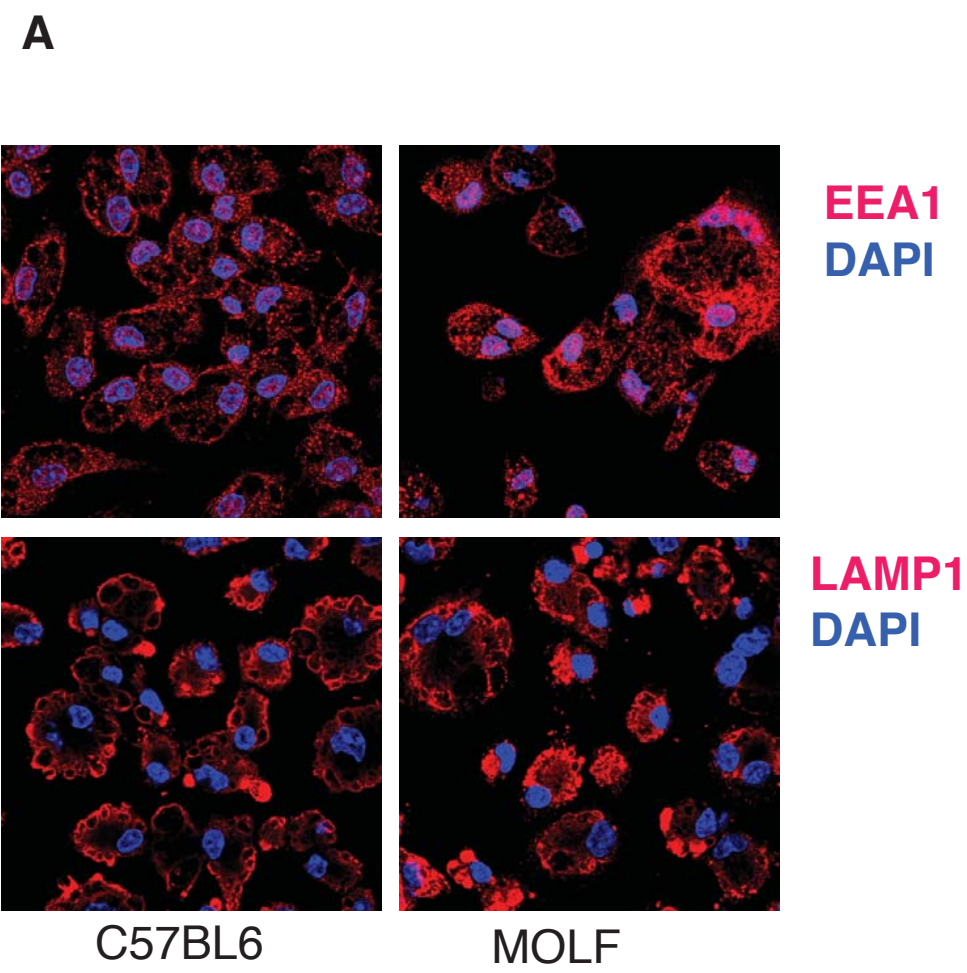
Figure S2



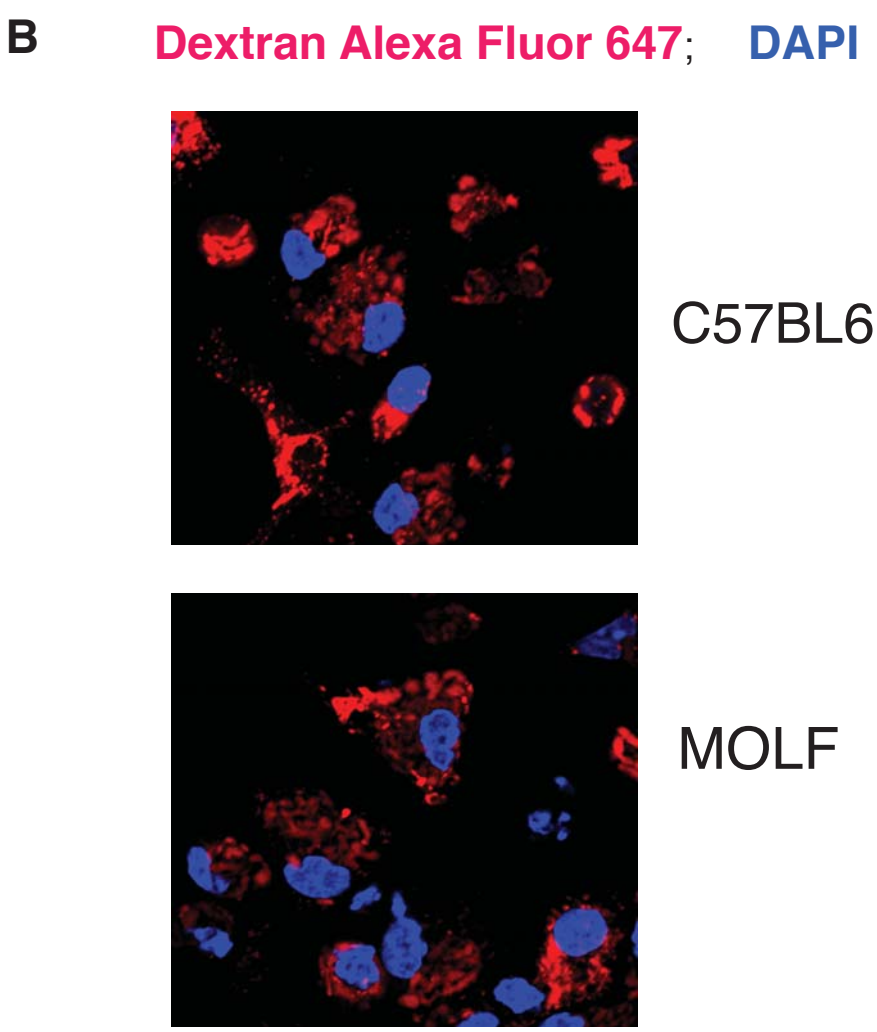


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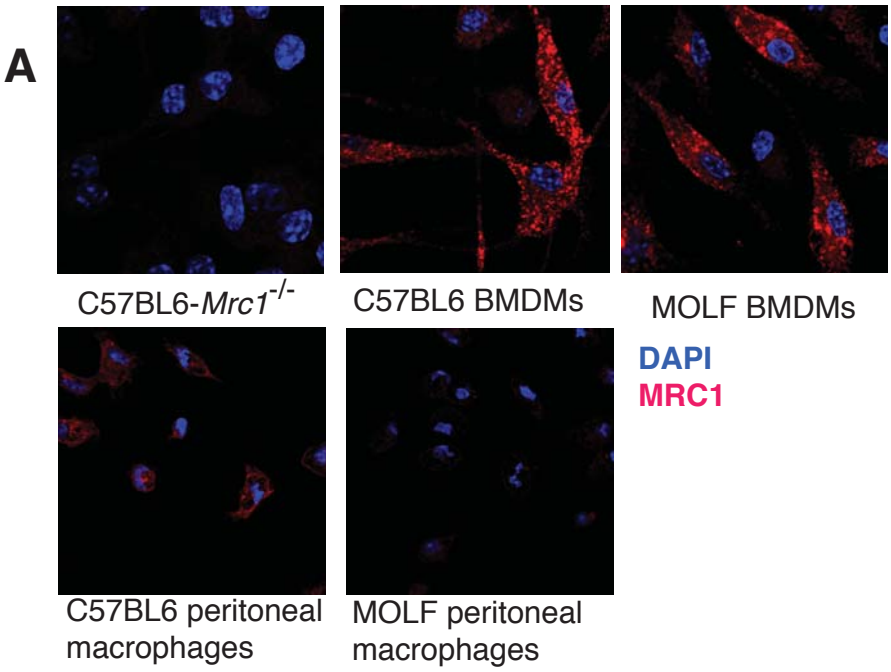
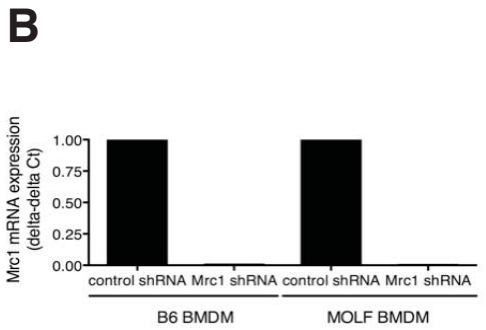
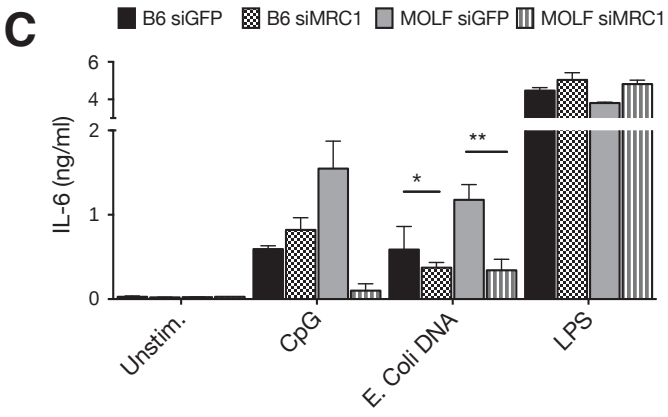
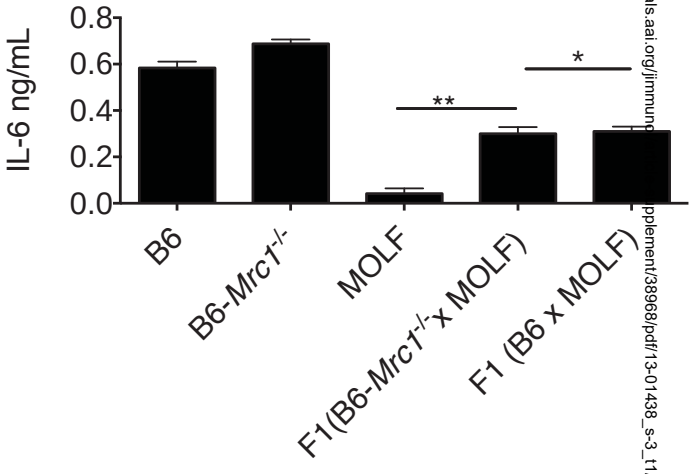
Figure S3









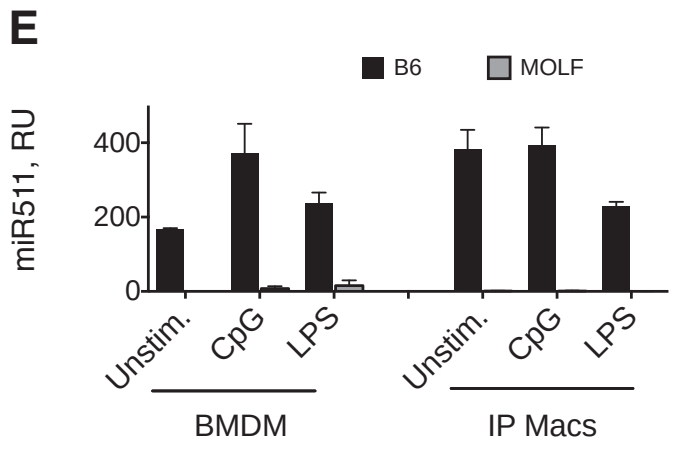


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Table S1: Asessment of cis-regulation of MRC1 allele using massive parallel RNA-sequencing

EXON #	SNP	aa/aa	position	Number of reads in F1/no LPS		log p-value	Number of reads in F1/LPS		log p-value
				B6	MOLF		B6	MOLF	
ENON 3	C/G	R/R	14,165,843	49	2	-11.92	43	7	-6.67
EXON 4	C/T	T/T	14,170,474	56	8	-9.25	36	13	-2.83
EXON 4	G/A	P/P	14,170,468	61	8	-10.38	34	15	-2.02
EXON 5	C/G	S/T	14,178,692	49	18	-3.71	94	6	-20.69
EXON 6	C/T	P/P	14,182,836	40	15	-2.99	57	10	-8.39
EXON 10	C/T	N/N	14,197,997	50	13	-5.52	49	9	-7.04
EXON 16	G/A	P/P	14,225,773	51	14	-5,35	46	2	-11,07
EXON 17	A/G	A/A	14,227,018	23	3	-4.05	17	0	-4.8
EXON 19	C/T	D/D	14,229,524	21	3	-3.55	23	4	-3.5
EXON 22	T/G	A/T	14,236,927	22	6	-2.40	29	2	-6.31
EXON 25	C/T	N/N	14,243,532	38	4	-7.24	41	7	-6.20
EXON 26	A/G	T/T	14,246,965	33	1	-8.39	36	2	-8.27
EXON 30	G/T	R/R	14,252,946	47	5	-8.89	39	7	-5.73

The RNA from not activated and LPS-activated macrophages from F1 hybrid mice was used in NGS (next generation sequencing) analysis to identify polymorphism (SNPs, column 2) in several exons of MRC1. For each SNP, we calculated the number of reads corresponding to either B6 or MOLF allele of MRC1 and used binomial distribution and null hypothesis to calculate p-value for the allelic expression of MRC1.

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SUPPLEMENTARY FIGURES LEGENDS

Supplemental Figure 1:

(A) MOLF/Ei peritoneal macrophages are responsive to LPS-free *E. coli* DNA: Peritoneal macrophages were activated with 10ng/mL *E. coli* DNA for 6 hours and IL-6 cytokine production was measured by ELISA. *E. coli* DNA was treated with DNase for 1 hour prior to activation with cells. Data are representative of three independent experiments; (**B) MOLF TLR9 is functional:** Peritoneal macrophages were activated with 200nM CpG for 6 hours and IL-6 was measured by ELISA. Data are representative of five independent experiments; (**C) Inflammatory cytokine production in peritoneal macrophages from B6, MOLF/Ei and F1 (B6xMOLF/Ei) mice**: TNF-a, IL-12p40, IL-10 and IL-6 cytokine production in response to 200nM CpG activation at indicated time points was measured by real time PCR using taqman based probes in peritoneal macrophages. Data are representative of at least three independent experiments.

Supplemental Figure 2:

(A) B6 and MOLF peritoneal macrophages have comparable EEA1 and LAMP1 expression: Peritoneal macrophages were stained with EEA1 and LAMP1 specific antibodies. Staining was visualized by confocal microscopy. Images are representative of at least three independent experiments imaging a total of at least 75 cells per experiment; (**B) B6 and MOLF peritoneal macrophages take up and traffic dextran similarly.** Labeled dextran was used to visualize macrophage uptake and endolysosomal trafficking by confocal microscopy. Peritoneal macrophages were incubated with Alexa Fluor 647 dextran for 20 minutes at 37^{o}C, 5% CO_2. Images are representative of at least three independent experiments imaging a total of at least 75 cells per experiment.

Supplemental Figure 3:

(A) Mannose receptor staining in B6 and MOLF macrophage populations: Bone-marrow derived macrophages and peritoneal macrophages were stained with mannose receptor antibody (clone MR5D3). Protein expression was visualized using confocal microscopy. Images are representative of at least three independent experiments imaging a total of at least 75 cells per experiment; **(B) Mrc1 lentiviral knockdown efficiency in BMDMs:** Knockdown efficiency was measured by real-time PCR using taqman specific probes for *Mrc1.* Relative *Mrc1* expression levels were compared between control shRNA and *Mrc1* shRNA transduced samples to determine knockdown efficiency. Data are representative of at least three independent experiments; **(C) Mrc1 is required for responses to bacterial DNA in MOLF/Ei macrophages:** B6 and MOLF BMDMs were infected with lentivirus encoding siGFP- or siMRC1-specific shRNA hairpins. IL6 levels were measured after 6 hours of activation with 200nM CpG , 10µg E.coli DNA or 100 ng/ml of LPS. Data are representative of two independent experiments. * - $p>0.05$; ** - $p<0.01$**; (D) Mannose receptor is dispensible for C57BL/6 CpG responses:** Peritoneal macrophages were activated with 200nM CpG for 6 hours. IL-6 cytokine response was measured by ELISA. **(E)** Levels of miR511 were compared by means of Q-PCR in bone-

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marrow derived (BMDM) and peritoneal (IP) B6 and MOLF macrophages upon their stimulation with LPS or CpG. Data are representative of at least three independent experiments. * - $p>0.05$; ** - $p<0.001$

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