Supplementary Table1 Hematological profile of mice injected with 500ug LPS for 4 hours, 100 ug PolyI:C daily for 5 days, with 1000 CFUs I.V. of *Salmonella* Typhimurium or with control PBS. PolyI:C induced a lymphopenia, monocytopenia and thrombocytopenia in Ity9 mice.

Supplementary Figure 1 Initial mapping of the Ity9 mutation to two potential chromosomal locations (6 and 14) using 6 affected mice (225, 227, 245, 246, 247, 248). 129S1 alleles are represented in red, C57BL/6J alleles in blue and heterozygous regions in yellow. LOD score to the right of the red line are considered significant.

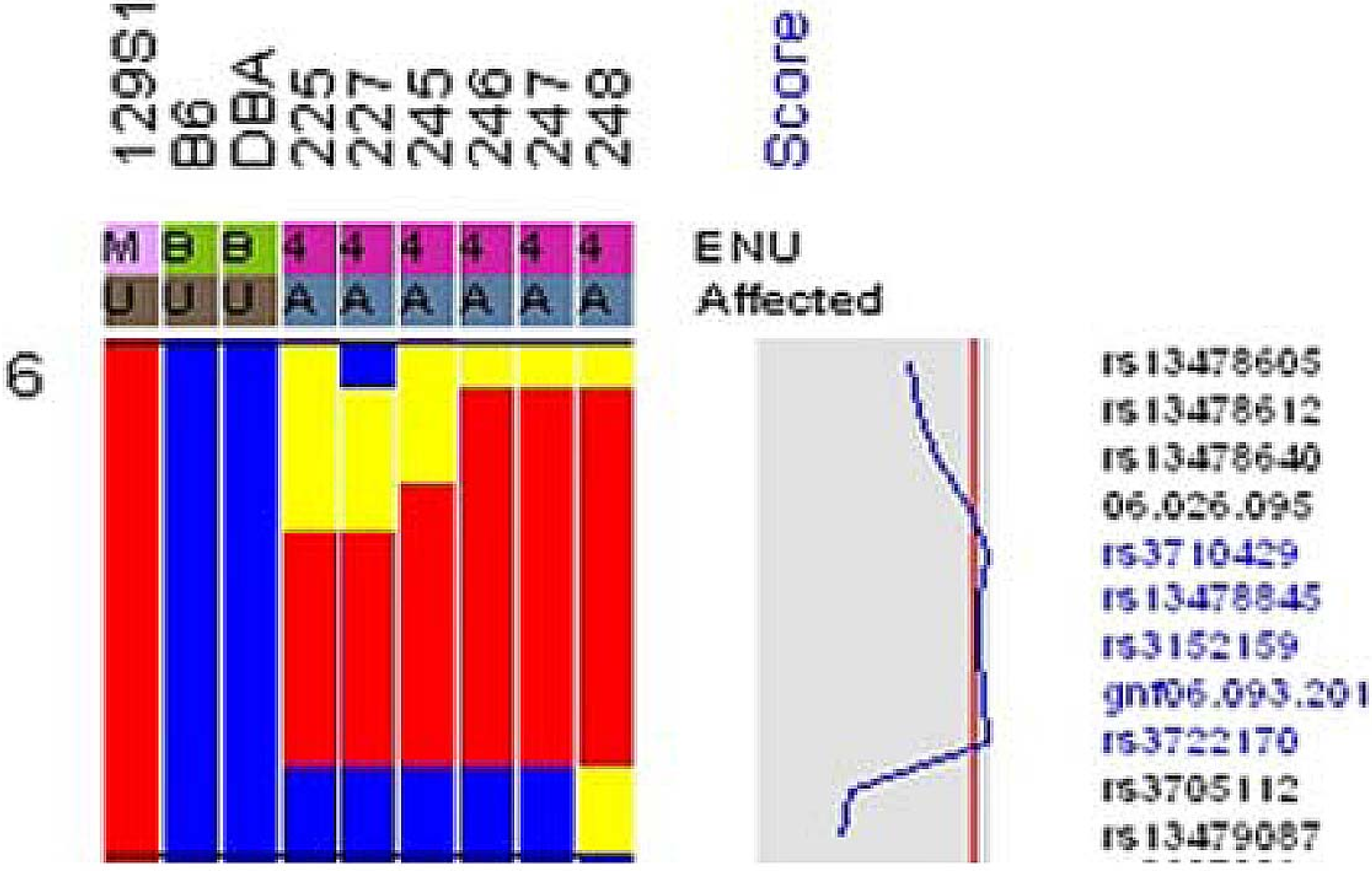
Supplementary Figure 2

Clustergrams of differentially regulated genes in the spleens (a) and BMDM (b) of $Usp18^{Ity9}/Usp18^{Ity9}$ and $Usp18^{Ity9}/Usp18^{\mathrm{wt}}$ littermates generated using the Web based RT2 Profiler PCR Array Data Analysis (sabiosciences.com/pcr/arrayanalysis.php). (a) Spleens were harvested at day 6 post-infection with 1000 CFUs of *Salmonella* Typhimurium. (b) BMDM were infected *in vitro* at a 10:1 ratio with *Salmonella* Typhimurium. Following mRNA extraction using RNeasy Mini Kit (Qiagen, Missisauga ON), the gene expression was evaluated using the RT^{2}Profiler PCR Array: Mouse Interferon and Receptors (SABioscience, Frederick MD).

Supplementary Figure 3

Gene expression validation. QRT-PCR analysis of differentially regulated genes in the spleens (a,b) and BMDM (c,d) of $Usp18^{Ity9}/Usp18^{Ity9}$ and $Usp18^{Ity9}/Usp18^{\mathrm{wt}}$ littermates. Expression ratios represents the relative expression of the $Usp18^{Ity9}/Usp18^{Ity9}$ mice compared to the $Usp18^{Ity9}/Usp18^{\mathrm{wt}}$ mice. Amplification data was done with Chromo4 apparatus (Bio-Rad, Missisauga) using Brillant SYBR green QPCR Master Mix (Stratagene). The data was analyzed using Rest2008 software (Corbett Research, Sydney) and is presented as whisker box plot. Randomization test with 10 000 iterations were performed. (a,b) Spleens were harvested at day 6 post-infection with 1000 CFUs of *Salmonella* Typhimurium. (c,d) BMDM were infected *in vitro* at a 10:1 ratio with *Salmonella* Typhimurium. Randomization test results: (a) *Ifng* $P<0.0001$, *Irf7* $P=0.05$, *Irf8* $P<0.0001$, (b) *Ifng* $P=0.001$, *Il6* $P=0.001$, *Cxcl10* $P=0.001$, *Irf7* $P<0.0001$, (c) *Ifnb1* $P=0.001$, *Il15* $P=<0.0001$, *Isg15* $P<0.0001$, *Mx1* $P=0.001$, (d) *Ifnb1* $P=0.05$. Results are representative of two experiments. Primer sequence: *Ifnb1* 5’-CCCTATGGAGATGACGGAGA-3, 5’-TCCCACGTCAATCTTTCCTC-3’, *Cxcl10* 5’-TCTGAGTGGGACTCAAGGG-3’, 5’-TAAGGAGCCCTTTTAGACCTT-3’, *Irf7* 5’-AGCACTTTCTTCCGAGAACTG-3’, 5’-TAGACAAGCACAAGCCGAGA-3’, *Irf8* 5’-ATGCTTCCATCTTCAAGGCC-3’, 5’-CCCAGCTTGCATTTTTGTTC-3’, *Isg15* 5’-AGAGCCTGCAGCAATGGC-3’, 5’-TCGCTGCAGTTCTGTACCA-3’, *Ifng* 5’-ACTGGCAAAAGGATGGTGAC-3’, 5’-ATCCTTTTTCGCCTTGCTGT-3’, *Il6* 5’-GAGCCCACCAAGAACGATAG-3’, 5’-TCCACGATTTCCCAGAGAAC-3’, *Il15* 5’-TTGCAGTGCATCTCCTTACG-3’, 5’-GTGCTTTGAAGAGCCAGAGG-3’, *Mx1* 5’-CCCAGAGGCAGTGGTATTGT-3’, 5’-ACATTTGGGGAGCTGACATC-3’.

	PBS			**LPS 4h**			**PolyI:C**			**Salmonella D5**		
	Wt (n=3)	Ity9 (n=3)	*P*	Wt (n=3)	Ity9 (n=3)	*P*	Wt (n=3)	Ity9 (n=3)	*P*	Wt (n=3)	Ity9(n=3)	*P*
Hematocrit	0.49±0.01	0.51±0.04	0.39	0.49±0.02	0.50±0.41	0.41	0.45±0.02	0.42±0.03	0.26	0.42±0.01	0.39±0.02	0.09
WBCx10^9	6.87±0.60	7.30±2.38	0.78	5.23±1.31	4.33±0.92	0.38	9.47±2.52	5.53±1.43	0.08	10.23±2.4	4.70±1.4	0.03
Neutrox10^9	1.52±0.21	1.51±0.96	0.99	1.26±0.41	1.54±0.12	0.32	1.62±0.65	2.24±0.76	0.34	3.22±1.6	0.88±0.44	0.07
Lymphox10^9	4.84±0.53	5.18±2.68	0.84	3.73±1.62	2.51±0.60	0.29	6.86±2.06	3.21±1.11	0.05	6.19±0.15	3.46±0.81	0.01
Monox10^9	0.35±0.15	0.53±0.68	0.68	0.06±0.05	0.14±0.11	0.30	0.75±0.20	0.07±0.08	0.01	0.57±0.37	0.36±0.33	0.51
Plateletsx10^{11}	9.04±1.22	6.07±3.87	0.28	5.64±0.78	5.06±2.67	0.73	8.22±2.42	1.14±0.15	0.01	3.71±1.58	2.22±0.62	0.20


129S1
B6
DBA
225
227
245
246
247
248
Score
M
B
B
4
4
4
4
4
4
ENU
U
U
U
A
A
A
A
A
A
Affected
6
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rs13478612
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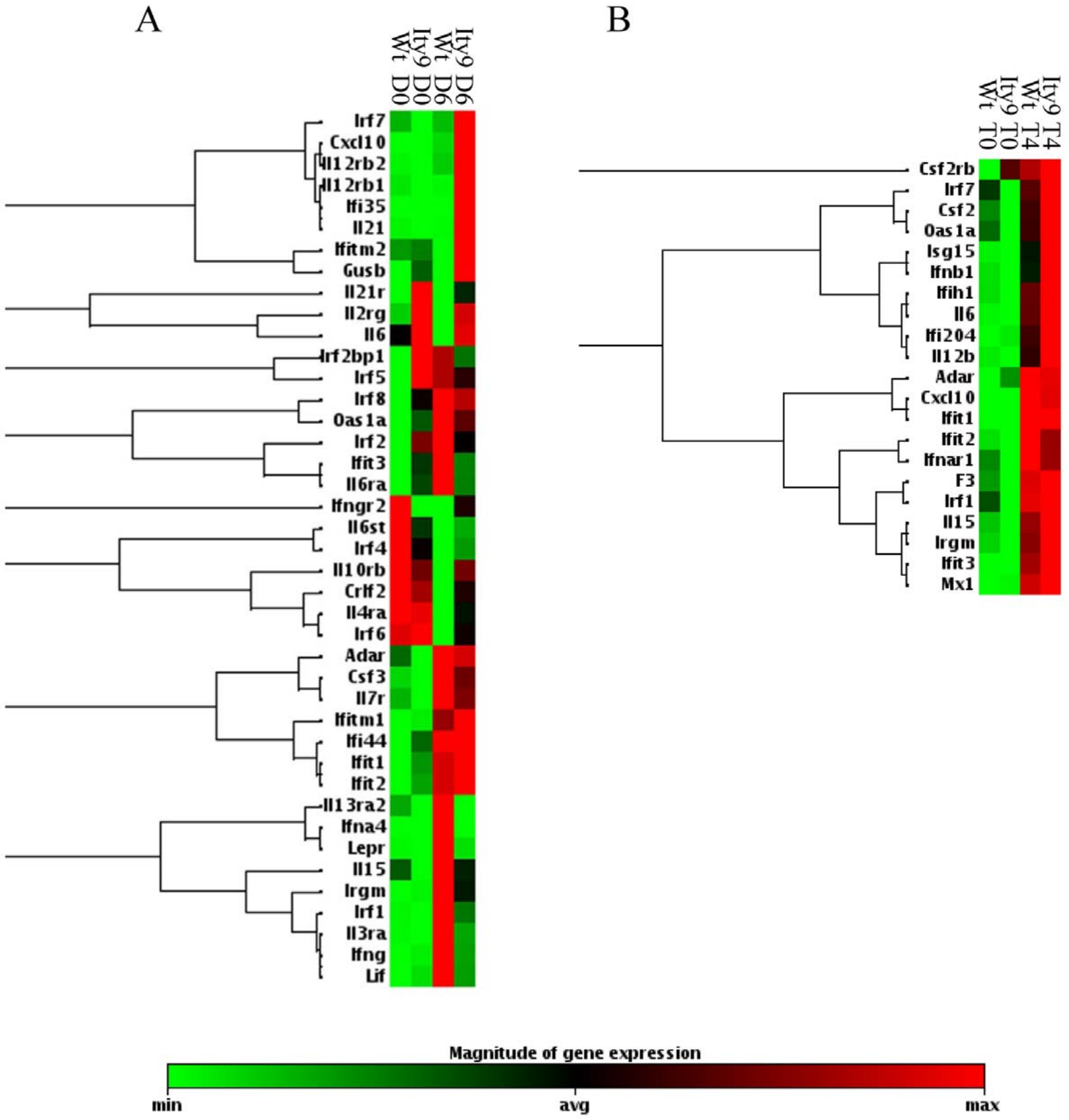
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Wt D0
Ity9 D0
Wt D6
Ity9 D6
Irf7
Cxcl10
Il12rb2
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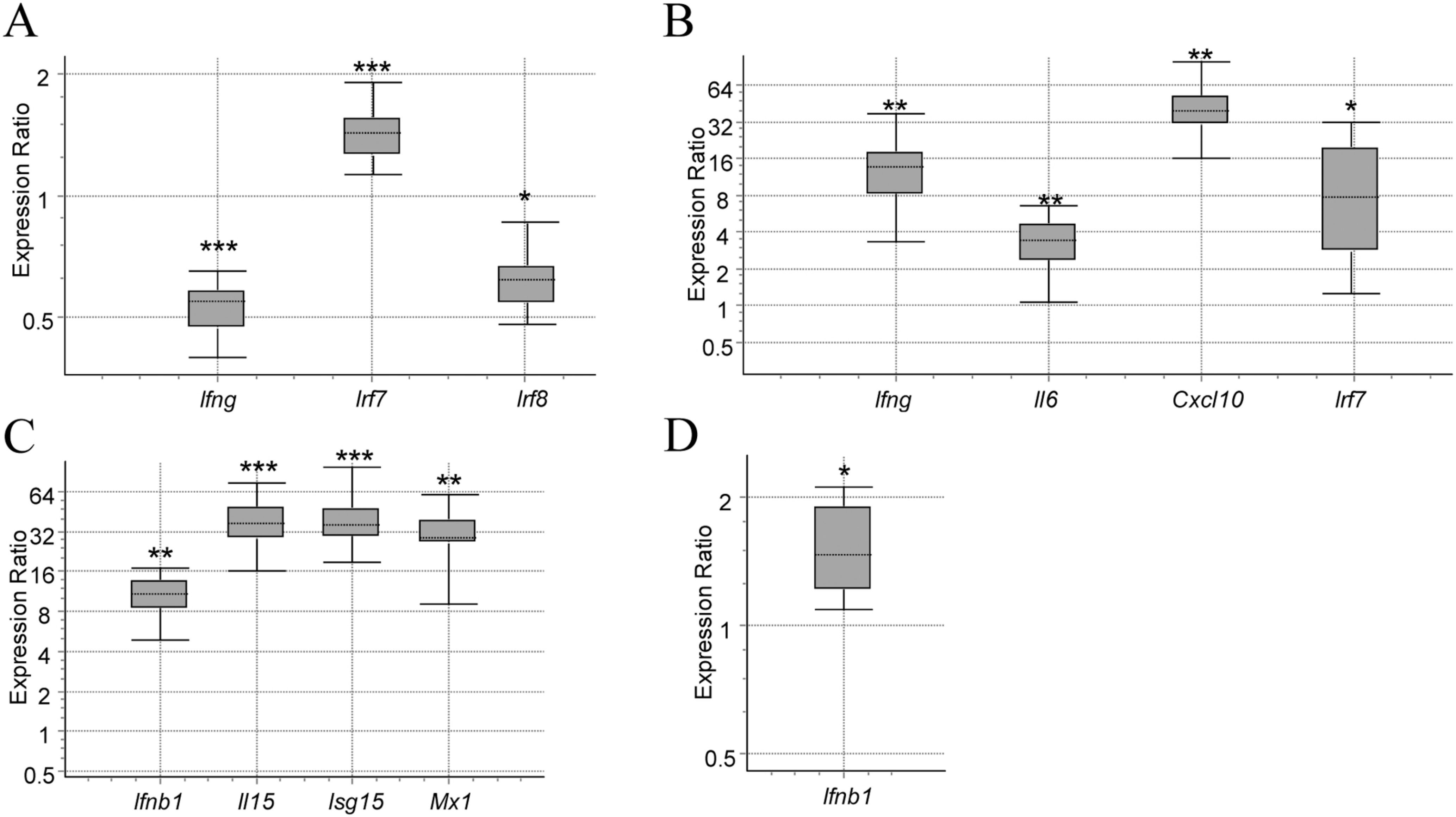
Gusb
Il21r
Il2rg
Il6
Irf2bp1
Irf5
Irf8
Oas1a
Irf2
Ifit3
Il6ra
Ifngr2
Il6st
Irf4
Il10rb
Crlf2
Il4ra
Irf6
Adar
Csf3
Il7r
Ifitm1
Ifi44
Ifit1
Ifit2
Il13ra2
Ifna4
Lepr
Il15
Irgm
Irf1
Il3ra
Ifng
Lif
B
Wt T0
Ity9 T0
Wt T4
Ity9 T4
Csf2rb
Irf7
Csf2
Oas1a
Isg15
Ifnb1
Ifih1
Il6
Ifi204
Il12b
Adar
Cxcl10
Ifit1
Ifit2
Ifnar1
F3
Irf1
Il15
Irgm
Ifit3
Mx1
Magnitude of gene expression
min
avg
max


A
Expression Ratio
2
1
0.5
***
***
*
Ifng
Irf7
Irf8
B
Expression Ratio
64
32
16
8
4
2
1
0.5
**
**
**
*
Ifng
Il6
Cxcl10
Irf7
C
Expression Ratio
64
32
16
8
4
2
1
0.5
**
***
***
**
Ifnb1
Il15
Isg15
Mx1
D
Expression Ratio
2
1
0.5
*
Ifnb1