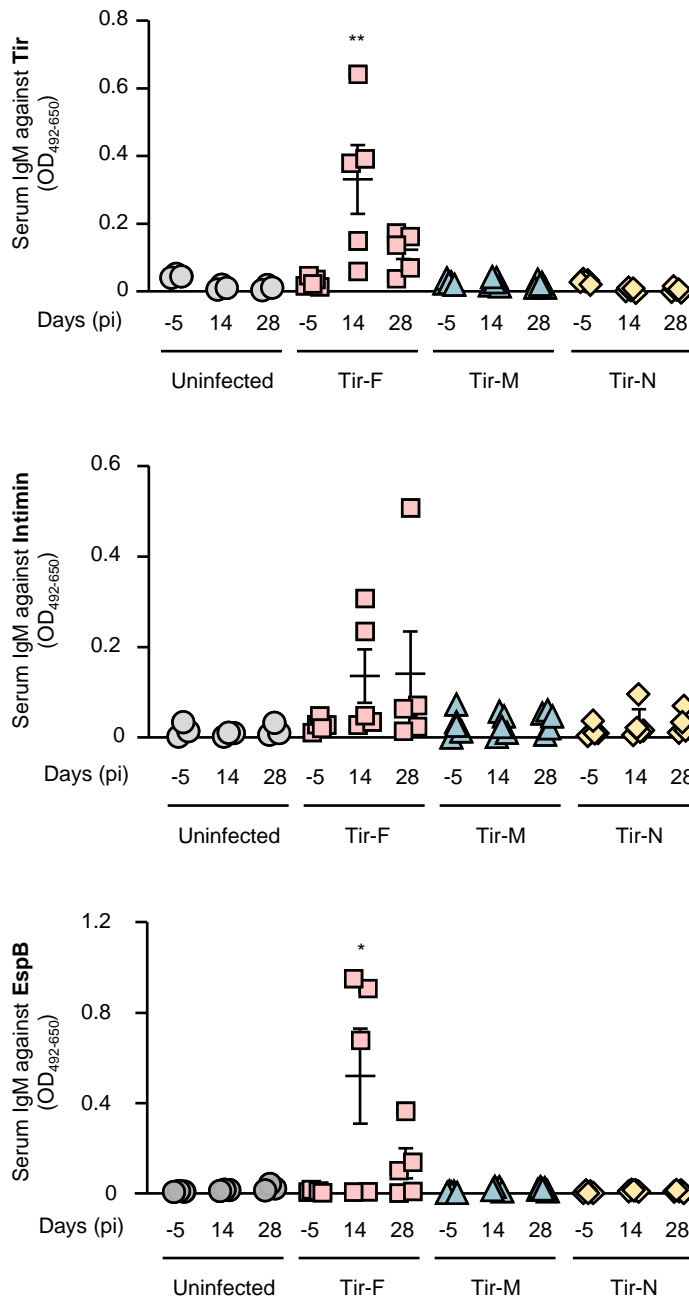


## Supplemental Figure 1

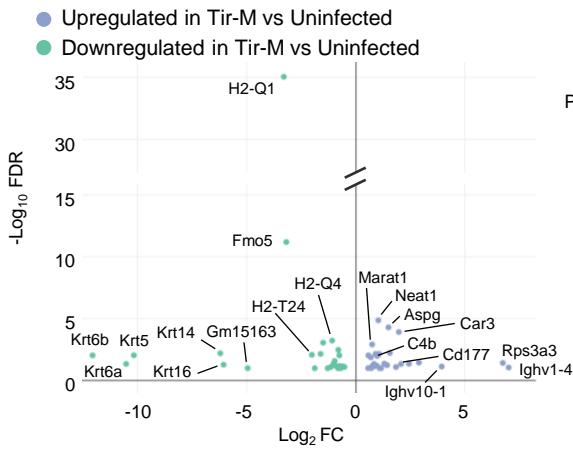


### Supplemental Figure 1. IgM antibody titers against virulence factors.

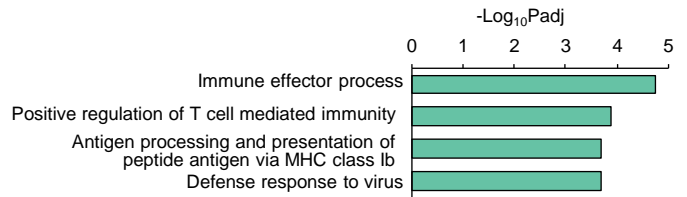
Mice were infected orally with Tir-F, -M, -N, or uninfected. The levels of serum IgM against Tir, Intimin, and EspB were determined by ELISA (means  $\pm$  SEM,  $n = 3-5$ ). Significance was determined by the Kruskal-Wallis test and Dunnett post hoc test. \*  $p$ -value  $< 0.05$ , \*\*  $p$ -value  $< 0.01$ . Data from one representative experiment of two independent experiments are shown.

## Supplemental Figure 2

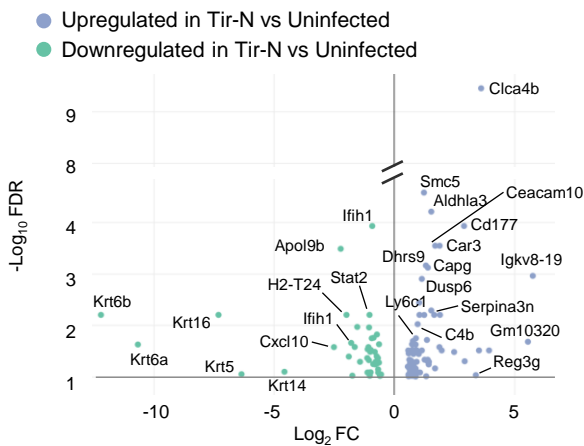
### A Tir-M vs. Uninfected



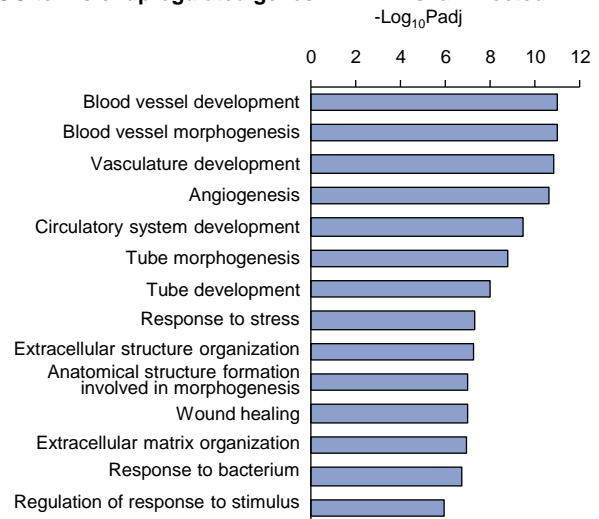
### D GO terms of downregulated genes in Tir-M vs. uninfected



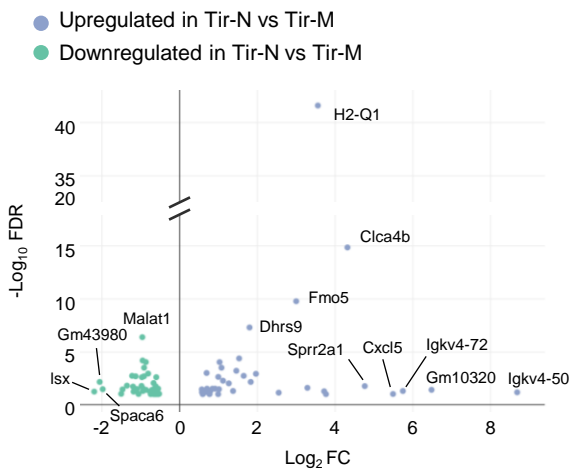
### B Tir-N vs. Uninfected



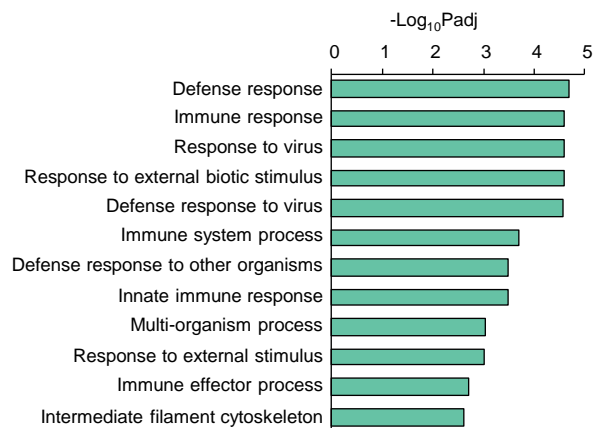
### E GO terms of upregulated genes in Tir-N vs. uninfected



### C Tir-N vs. Tir-M



### F GO terms of downregulated genes in Tir-N vs. uninfected



**Supplemental Figure 2. DEG and Gene Ontology (GO) analyses of Tir-M- or Tir-N-infected mice.** Volcano plots of DEGs. (A) Tir-M-infected vs. Uninfected groups, (B) Tir-N-infected vs. Uninfected groups, and (C) Tir-N- vs. Tir-M-infected groups. (D) GO analysis of genes downregulated in Tir-M-infected mice compared to those in uninfected mice. (E, F) GO analysis of genes upregulated (E) or downregulated (F) in Tir-N-infected mice compared to those in the uninfected mice. The X-axis indicates  $-\log_{10}$  adjusted P values ( $P_{adj}$ ), and the y-axis indicates enriched biological processes.

**Supplemental Table 1. Primer sets used for RT-qPCR.**

Gene	Forward primer (5' to 3')	Reverse primer (5' to 3')	Ref.
<i>ler</i>	GAGCAGGAGATTCAAACGT	TACCCCAGTTCTTGTAAAGGT	14
<i>espB</i>	CGCAAAGCTATAACATCCAAC	AGCCTAAAATCCCCAGGAC	this study
<i>Tir</i>	GCTTCCTGAACATCCATTGC	ACCTCTACACCATCTTTTACCC	this study
<i>ces-T</i>	GGTTTGCAGAGAATGGTGGAC	AACGTCATCGAGAGGGAAACG	this study
<i>eae</i>	TTATTCATGGTTTTTGCACC	AAAACAATCCTAAACCAGCA	14
<i>nanoluc</i>	ACCTGGACCAAGTCCTTGAAC	TCAGCCCATTTTCACCGCTC	this study
<i>Saa3</i>	GCAACTACTGGGTTGAGATA	ATTCAGCACATTGGGATG	10
<i>Saa4</i>	AGGAGAGAGAAAGCAGCAG	CAAGCCTCATGATGCGACTC	this study
<i>Cxcl1</i>	TGGCTGGGATTCACCTCAAGAAC	TGTGGCTATGACTTCGGTTTGGGT	19
<i>IL-17A</i>	TTTAACTCCCTTGGCGCAAAA	CTTTCCCTCCGCATTGACAC	<sup>a</sup>
<i>Plet1</i>	CGTGGTCCTTGATAACATCT	TCACGGCACTGACTGAA	26
<i>Nos2</i>	TTCAGCACATCTGCAGACAC	AGCCTGAAGTCATGTTTGCC	10
<i>Gapdh</i>	GTCGTGGAGTCTACTGGTGTCTTC	GTCATATTTCTCGTGGTTCACACC	10

<sup>a</sup> found in: [Ishigame, H., S. Kakuta, T. Nagai, M. Kadoki, A. Nambu, Y. Komiyama, N. Fujikado, Y. Tanahashi, A. Akitsu, H. Kotaki, et al. 2009. Differential roles of interleukin-17A and -17F in host defense against mucoc epithelial bacterial infection and allergic responses. *Immunity* 30: 108.119.]

**Supplemental Table 2. Selected DEGs involved in immune responses that were increased in Tir-F-infected mice.**

Gene	Description	Gene expression (FPKM)							
		U_1	U_2	Tir-F_1	Tir-F_2	Tir-M_1	Tir-M_2	Tir-N_1	Tir-N_2
<i>Saa3</i>	serum amyloid A 3	0.14	0.16	1.16	3.86	0.09	0.05	0.45	0.49
<i>Saa4</i>	serum amyloid A 4	0.00	0.10	0.31	0.70	0.00	0.00	0.00	0.00
<i>Plet1</i>	placenta expressed transcript 1	0.13	0.70	226.25	210.89	0.71	0.56	0.84	1.10
<i>Cxcl1</i>	chemokine (C-X-C motif) ligand 1	0.00	0.00	3.39	3.41	0.00	0.13	1.00	0.26
<i>Cxcl2</i>	chemokine (C-X-C motif) ligand 2	0.00	0.00	1.09	1.92	0.00	0.00	0.17	0.05
<i>Cxcl5</i>	chemokine (C-X-C motif) ligand 5	0.13	0.00	5.14	11.13	0.00	0.00	0.81	0.26
<i>Cxcl9</i>	chemokine (C-X-C motif) ligand 9	0.85	0.62	7.82	5.17	0.81	0.77	0.70	0.68
<i>Cxcl13</i>	chemokine (C-X-C motif) ligand 13	6.72	15.47	46.07	31.05	11.48	21.51	19.78	25.38
<i>Ccl7</i>	chemokine (C-C motif) ligand 7	1.68	1.57	9.41	7.45	1.45	1.83	3.49	3.77
<i>Ccl8</i>	chemokine (C-C motif) ligand 8	1.20	2.25	30.55	28.89	2.49	3.58	8.45	4.19
<i>Ccr5</i>	chemokine (C-C motif) receptor 5	0.06	0.19	0.66	0.78	0.23	0.29	0.30	0.17
<i>Ccr10</i>	chemokine (C-C motif) receptor 10	0.21	0.24	3.18	3.28	0.74	0.71	0.54	0.73
<i>Cxcr2</i>	chemokine (C-X-C motif) receptor 2	0.00	0.00	0.18	0.45	0.11	0.04	0.27	0.26
<i>Duox2</i>	dual oxidase 2	9.90	7.06	51.74	50.16	9.10	8.56	15.19	12.96
<i>Duoxa2</i>	dual oxidase maturation factor 2	3.93	4.21	63.24	60.52	3.20	4.44	6.08	8.01
<i>Nos2</i>	nitric oxide synthase 2, inducible	0.25	0.71	69.14	45.38	0.26	0.58	0.79	0.60
<i>Ly6a</i>	lymphocyte antigen 6 complex, locus A	118.71	169.93	1473.42	1158.42	198.67	163.83	223.51	268.75
<i>Ly6c1</i>	lymphocyte antigen 6 complex, locus C1	12.57	12.23	99.20	143.00	15.19	18.24	22.19	23.91
<i>Cd177</i>	CD177 antigen	10.45	6.12	400.41	359.69	19.66	49.99	55.28	68.08
<i>Reg3b</i>	regenerating islet-derived 3 beta	0.00	0.00	4.24	5.96	0.10	0.11	0.00	2.13
<i>Reg3g</i>	regenerating islet-derived 3 gamma	0.17	0.10	3.77	5.10	0.22	0.06	0.22	2.58
<i>Cd4</i>	CD4 antigen	0.55	0.78	1.50	1.66	0.92	1.18	0.64	2.03
<i>Cd8a</i>	CD8 antigen, alpha chain	0.17	0.26	1.04	1.38	0.35	0.44	0.22	0.21
<i>Cd28</i>	CD28 antigen	0.28	0.12	0.81	0.79	0.23	0.34	0.23	0.25
<i>Gzma</i>	granzyme A	0.00	0.00	14.66	19.57	0.35	0.48	0.23	0.58
<i>Gzmb</i>	granzyme B	0.34	0.07	9.60	14.15	0.08	0.51	0.24	0.14
<i>Pla2g5</i>	phospholipase A2, group V	3.87	3.27	16.88	18.05	2.81	3.76	4.08	4.32
<i>Aicda</i>	activation-induced cytidine deaminase	0.14	0.12	0.93	0.51	0.70	0.28	0.31	0.18
<i>Tnfsf10</i>	tumor necrosis factor (ligand) superfamily, member 10	8.71	6.54	28.07	20.84	6.49	6.11	5.74	7.83
<i>Il17a</i>	interleukin 17A	0.00	0.00	1.20	1.16	0.00	0.00	0.00	0.00
<i>Il17f</i>	interleukin 17F	0.06	0.05	0.53	0.62	0.00	0.12	0.00	0.05
<i>Il21</i>	interleukin 21	0.00	0.00	0.10	0.04	0.00	0.00	0.00	0.00
<i>Igha</i>	immunoglobulin heavy constant alpha	26.37	284.14	947.33	807.64	205.46	124.87	160.93	177.04
<i>Ighm</i>	immunoglobulin heavy constant mu	10.92	25.63	82.44	49.58	36.79	41.74	24.24	44.06
<i>Ighg1</i>	immunoglobulin heavy constant gamma 1	0.24	1.53	4.07	3.03	0.67	0.71	0.63	1.61
<i>Ighg2b</i>	immunoglobulin heavy constant gamma 2B	0.46	1.09	68.88	27.65	3.16	2.32	1.52	6.58
<i>Ighg2c</i>	immunoglobulin heavy constant gamma 2C	0.09	0.16	8.69	3.32	0.35	0.09	0.09	0.15
<i>Ighg3</i>	immunoglobulin heavy constant gamma 3	0.05	0.54	2.40	1.50	1.38	2.38	0.46	1.94
<i>Jchain</i>	immunoglobulin joining chain	14.07	134.61	350.06	305.38	74.36	43.48	61.87	66.11
<i>Igkc</i>	immunoglobulin kappa constant	135.71	1214.91	3763.80	2785.27	676.20	511.26	645.27	783.77
<i>Ighv1-4</i>	immunoglobulin heavy variable 1-4	0.00	0.00	0.31	11.64	0.99	14.23	1.66	1.39
<i>Ighv1-26</i>	immunoglobulin heavy variable 1-26	0.35	0.00	0.61	17.30	0.00	9.03	4.32	8.87
<i>Ighv1-63</i>	immunoglobulin heavy variable V1-63	0.70	3.28	458.93	223.76	1.98	0.00	4.65	1.66
<i>Ighv2-6-8</i>	immunoglobulin heavy variable 2-6-8	0.00	0.00	1.23	1.20	0.00	0.00	4.33	13.07
<i>Ighv3-4</i>	immunoglobulin heavy variable V3-4	0.00	4.15	86.02	48.65	4.59	0.00	2.31	6.34
<i>Ighv3-6</i>	immunoglobulin heavy variable 3-6	1.75	17.04	59.68	63.43	8.60	5.92	16.00	9.73
<i>Ighv6-3</i>	immunoglobulin heavy variable 6-3	0.34	2.65	105.86	63.83	20.50	3.77	3.28	7.38
<i>Ighv8-8</i>	immunoglobulin heavy variable 8-8	0.34	0.00	0.00	3.51	2.91	9.19	0.00	0.82
<i>Ighv10-1</i>	immunoglobulin heavy variable 10-1	0.00	1.46	2.70	14.29	15.81	7.47	3.25	3.52
<i>Igkv1-135</i>	immunoglobulin kappa variable 1-135	0.00	2.12	13.94	49.17	0.00	0.00	3.26	3.70
<i>Igkv3-2</i>	immunoglobulin kappa variable 3-2	0.00	2.49	20.51	48.20	0.00	0.00	0.93	0.77
<i>Igkv3-7</i>	immunoglobulin kappa variable 3-7	0.34	4.37	18.90	52.80	3.23	1.36	3.90	1.36
<i>Igkv4-53</i>	immunoglobulin kappa variable 4-53	1.34	18.25	1297.10	345.83	3.16	4.32	1.27	7.95
<i>Igkv4-72</i>	immunoglobulin kappa chain variable 4-72	0.00	1.04	91.60	39.33	0.00	0.00	3.19	2.66
<i>Igkv6-13</i>	immunoglobulin kappa variable 6-13	0.00	1.17	90.58	9.92	0.97	1.02	0.32	0.54
<i>Igkv8-19</i>	immunoglobulin kappa variable 8-19	0.00	0.57	21.24	22.92	7.51	2.31	11.35	21.30
<i>Igkv8-24</i>	immunoglobulin kappa chain variable 8-24	0.00	6.59	20.36	27.26	14.60	6.34	1.60	5.07
<i>Igkv8-28</i>	immunoglobulin kappa variable 8-28	0.00	0.28	1.75	1.13	0.00	0.00	5.99	7.36
<i>Igkv12-44</i>	immunoglobulin kappa variable 12-44	1.53	2.61	34.91	13.84	5.20	3.95	5.82	12.62
<i>Iglv1</i>	immunoglobulin lambda variable 1	1.88	15.79	83.99	81.69	12.14	5.92	7.46	16.67
<i>Iglv3</i>	immunoglobulin lambda variable 3	0.97	2.47	10.74	6.05	3.65	4.48	0.92	2.55