

## RNA-seq Profiles of Immune Related Genes in the Spleen of Necrotic Enteritis-afflicted Chicken Lines

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### - Supplementary Data -

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#### Sequence data availability

All raw Illumina sequence data can be obtained freely by contacting the Department of Animal Science and Technology. The AMG\_Gallus database has been uploaded in the National Agricultural Biotechnology Information Center (NABIC, <http://nabic.rda.go.kr/>) [ID: NN-0915-000001 and NN-0915-000002].

**Supplementary Table S1a.** Gene ontology enrichment test in the spleen of resistant chicken line 6.3 with  $p < 0.05$  and Log2-transformations of the normalization  $\geq 2$  (MF: molecular function, BP: biological process and CC: cellular component). The data showed the number of genes which were up- and downregulated in resistant chicken line 6.3.

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
GO:0043169	MF	cation binding	13	4	6.14E-05
GO:0043167	MF	ion binding	13	4	6.27E-05
GO:0046872	MF	metal ion binding	12	4	0.000196789
GO:0008237	MF	metallopeptidase activity	3	1	0.000268084
GO:0004089	MF	carbonate dehydratase activity	2	0	0.000299687
GO:0004222	MF	metalloendopeptidase activity	2	1	0.00082792
GO:0004869	MF	cysteine-type endopeptidase inhibitor activity	2	0	0.000947924
GO:0052582	MF	(+)-menthofuran synthase activity	1	0	0.00174286
GO:0043825	MF	succinylornithine transaminase activity	1	0	0.00194545
GO:0016705	MF	oxidoreductase activity, acting on paired donors, with incorporation or reduction of molecular oxygen	3	0	0.00196149
GO:0004026	MF	alcohol O-acetyltransferase activity	0	1	0.0019911
GO:0034318	MF	alcohol O-acyltransferase activity	0	1	0.0019911
GO:0034319	MF	alcohol O-butanoyltransferase activity	0	1	0.0019911
GO:0034323	MF	O-butanoyltransferase activity	0	1	0.0019911
GO:0034326	MF	butanoyltransferase activity	0	1	0.0019911
GO:0034338	MF	short-chain carboxylesterase activity	0	1	0.0019911
GO:0016836	MF	hydro-lyase activity	2	0	0.00296521
GO:0004611	MF	phosphoenolpyruvate carboxykinase activity	1	0	0.00343723
GO:0004613	MF	phosphoenolpyruvate carboxykinase (GTP) activity	1	0	0.00343723
GO:0005499	MF	vitamin D binding	1	0	0.0034967
GO:0016829	MF	lyase activity	1	1	0.00366269
GO:0004566	MF	beta-glucuronidase activity	1	0	0.00397161
GO:0045294	MF	alpha-catenin binding	1	0	0.00420115
GO:0046914	MF	transition metal ion binding	8	1	0.00445236
GO:0003824	MF	catalytic activity	18	10	0.00447815
GO:0070011	MF	peptidase activity, acting on L-amino acid peptides	3	2	0.00454432
GO:0016835	MF	carbon-oxygen lyase activity	2	0	0.00464331
GO:0005509	MF	calcium ion binding	3	2	0.00475453
GO:0003674	MF	molecular_function	28	7	0.00478706
GO:0008743	MF	L-threonine 3-dehydrogenase activity	1	0	0.00482599
GO:0008233	MF	peptidase activity	3	2	0.0050348
GO:0035529	MF	NADH pyrophosphatase activity	1	0	0.00510374
GO:0070573	MF	metalloendopeptidase activity	1	0	0.0051373
GO:0004668	MF	protein-arginine deiminase activity	0	1	0.00537643
GO:0015204	MF	urea transmembrane transporter activity	1	0	0.00548746
GO:0042887	MF	amide transmembrane transporter activity	1	0	0.00548746
GO:0005506	MF	iron ion binding	3	0	0.00550626
GO:0046996	MF	oxidoreductase activity, acting on paired donors	1	0	0.0058867
GO:0050046	MF	lathosterol oxidase activity	1	0	0.0058867
GO:0070704	MF	sterol desaturase activity	1	0	0.0058867
GO:0047756	MF	chondroitin 4-sulfotransferase activity	1	0	0.00624023
GO:0032217	MF	riboflavin transporter activity	1	0	0.00640645
GO:0004175	MF	endopeptidase activity	2	2	0.00718106
GO:0008239	MF	dipeptidyl-peptidase activity	1	0	0.00731233
GO:0004497	MF	monooxygenase activity	2	0	0.00792078
GO:0005215	MF	transporter activity	5	1	0.00913711
GO:0004528	MF	phosphodiesterase I activity	1	0	0.00952365
GO:0005184	MF	neuropeptide hormone activity	1	0	0.0108094
GO:0001968	MF	fibronectin binding	0	1	0.0119692
GO:0016813	MF	hydrolase activity, acting on carbon-nitrogen	0	1	0.0141259
GO:0022857	MF	transmembrane transporter activity	5	0	0.014237
GO:0004551	MF	nucleotide diphosphatase activity	1	0	0.0149732
GO:0016805	MF	dipeptidase activity	1	0	0.0152864
GO:0004866	MF	endopeptidase inhibitor activity	2	0	0.0175173
GO:0061135	MF	endopeptidase regulator activity	2	0	0.0177896
GO:0034481	MF	chondroitin sulfotransferase activity	1	0	0.018335
GO:0009055	MF	electron carrier activity	2	0	0.0185937
GO:0015116	MF	sulfate transmembrane transporter activity	1	0	0.0187158
GO:0051183	MF	vitamin transporter activity	1	0	0.0190009
GO:0047429	MF	nucleoside-triphosphate diphosphatase activity	1	0	0.0194876

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
GO:0019842	MF	vitamin binding	2	0	0.0201883
GO:0043027	MF	cysteine-type endopeptidase inhibitor activity involved in apoptotic process	1	0	0.0210609
GO:0017171	MF	serine hydrolase activity	0	2	0.021913
GO:0020037	MF	heme binding	2	0	0.0225592
GO:0030414	MF	peptidase inhibitor activity	2	0	0.0231552
GO:0016787	MF	hydrolase activity	5	4	0.0245724
GO:0016491	MF	oxidoreductase activity	4	0	0.0252204
GO:0045296	MF	cadherin binding	1	0	0.0255924
GO:0046906	MF	tetrapyrrole binding	2	0	0.0259168
GO:0061134	MF	peptidase regulator activity	2	0	0.029062
GO:0015291	MF	secondary active transmembrane transporter activity	2	0	0.0301934
GO:0016413	MF	O-acetyltransferase activity	0	1	0.0309025
GO:0015301	MF	anion:anion antiporter activity	1	0	0.0311367
GO:0008009	MF	chemokine activity	0	1	0.0324486
GO:0043499	MF	eukaryotic cell surface binding	0	1	0.0332507
GO:0042379	MF	chemokine receptor binding	0	1	0.0339999
GO:0005488	MF	binding	20	5	0.0367398
GO:0005328	MF	neurotransmitter:sodium symporter activity	0	1	0.0373173
GO:0022891	MF	substrate-specific transmembrane transporter activity	5	0	0.0394981
GO:0043028	MF	cysteine-type endopeptidase regulator activity involved in apoptotic process	1	0	0.0409408
GO:0008483	MF	transaminase activity	1	0	0.0418697
GO:0016709	MF	oxidoreductase activity, acting on paired donors,	1	0	0.0433748
GO:0072341	MF	modified amino acid binding	1	0	0.0439676
GO:0005326	MF	neurotransmitter transporter activity	0	1	0.0451888
GO:0004091	MF	carboxylesterase activity	0	1	0.0454664
GO:0016769	MF	transferase activity, transferring nitrogenous groups	1	0	0.0469751
GO:0004857	MF	enzyme inhibitor activity	2	0	0.0470614
GO:0016831	MF	carboxy-lyase activity	1	0	0.0491927
GO:0019752	BP	carboxylic acid metabolic process	4	2	0.000212763
GO:0043436	BP	oxoacid metabolic process	4	2	0.000212763
GO:0006082	BP	organic acid metabolic process	4	2	0.000217525
GO:0042180	BP	cellular ketone metabolic process	4	2	0.000253846
GO:0016114	BP	terpenoid biosynthetic process	2	0	0.000543184
GO:0016054	BP	organic acid catabolic process	2	1	0.000978565
GO:0046395	BP	carboxylic acid catabolic process	2	1	0.000978565
GO:0006520	BP	cellular amino acid metabolic process	3	1	0.00120223
GO:0006721	BP	terpenoid metabolic process	2	0	0.00128429
GO:0044282	BP	small molecule catabolic process	2	1	0.0015781
GO:0008299	BP	isoprenoid biosynthetic process	2	0	0.00185047
GO:0071705	BP	nitrogen compound transport	2	1	0.00190925
GO:0051792	BP	medium-chain fatty acid biosynthetic process	0	1	0.0019911
GO:0051793	BP	medium-chain fatty acid catabolic process	0	1	0.0019911
GO:0044106	BP	cellular amine metabolic process	2	2	0.00220763
GO:0021849	BP	neuroblast division in subventricular zone	1	0	0.00221879
GO:0030860	BP	regulation of polarized epithelial cell differentiation	1	0	0.00221879
GO:0030862	BP	positive regulation of polarized epithelial cell differentiation	1	0	0.00221879
GO:0009063	BP	cellular amino acid catabolic process	2	0	0.00279384
GO:0006720	BP	isoprenoid metabolic process	2	0	0.00354996
GO:0019087	BP	transformation of host cell by virus	0	1	0.00358255
GO:0006105	BP	succinate metabolic process	1	0	0.0036492
GO:0019545	BP	arginine catabolic process to succinate	1	0	0.0036492
GO:0009308	BP	amine metabolic process	2	3	0.00385351
GO:0051791	BP	medium-chain fatty acid metabolic process	0	1	0.00395518
GO:0021873	BP	forebrain neuroblast division	1	0	0.00417217
GO:0009310	BP	amine catabolic process	2	0	0.00424347
GO:0006567	BP	threonine catabolic process	1	0	0.00482599
GO:0019518	BP	L-threonine catabolic process to glycine	1	0	0.00482599
GO:0050667	BP	homocysteine metabolic process	1	0	0.00527964
GO:0000052	BP	citrulline metabolic process	0	1	0.00537643
GO:0018101	BP	peptidyl-citrulline biosynthetic process from peptidyl-arginine	0	1	0.00537643
GO:0019240	BP	citrulline biosynthetic process	0	1	0.00537643
GO:0071918	BP	urea transmembrane transport	1	0	0.00548746
GO:0015816	BP	glycine transport	0	1	0.00553173
GO:0071460	BP	cellular response to cell-matrix adhesion	0	1	0.00555438
GO:0071404	BP	cellular response to low-density lipoprotein particle stimulus	0	1	0.00577902

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
<a href="#">GO:0043627</a>	BP	response to estrogen stimulus	0	2	0.00613608
<a href="#">GO:0032218</a>	BP	riboflavin transport	0	1	0.00640645
<a href="#">GO:0009068</a>	BP	aspartate family amino acid catabolic process	0	1	0.00650831
<a href="#">GO:0016053</a>	BP	organic acid biosynthetic process	1	2	0.00653598
<a href="#">GO:0046394</a>	BP	carboxylic acid biosynthetic process	1	2	0.00653598
<a href="#">GO:0030859</a>	BP	polarized epithelial cell differentiation	1	0	0.00681453
<a href="#">GO:0032328</a>	BP	alanine transport	0	1	0.0070819
<a href="#">GO:0008150</a>	BP	biological_process	26	8	0.00731891
<a href="#">GO:0071402</a>	BP	cellular response to lipoprotein particle stimulus	0	1	0.00777455
<a href="#">GO:0055098</a>	BP	response to low-density lipoprotein particle stimulus	0	1	0.00821599
<a href="#">GO:0015840</a>	BP	urea transport	1	0	0.00867569
<a href="#">GO:0006527</a>	BP	arginine catabolic process	1	0	0.00872043
<a href="#">GO:0006566</a>	BP	threonine metabolic process	1	0	0.00882713
<a href="#">GO:0044281</a>	BP	small molecule metabolic process	6	2	0.00909546
<a href="#">GO:0015824</a>	BP	proline transport	0	1	0.00951104
<a href="#">GO:0006722</a>	BP	triterpenoid metabolic process	1	0	0.00954903
<a href="#">GO:0016104</a>	BP	triterpenoid biosynthetic process	1	0	0.00954903
<a href="#">GO:0019742</a>	BP	pentacyclic triterpenoid metabolic process	1	0	0.00954903
<a href="#">GO:0019745</a>	BP	pentacyclic triterpenoid biosynthetic process	1	0	0.00954903
<a href="#">GO:0021591</a>	BP	ventricular system development	1	0	0.009551
<a href="#">GO:0021670</a>	BP	lateral ventricle development	1	0	0.009551
<a href="#">GO:0055094</a>	BP	response to lipoprotein stimulus	0	1	0.0102067
<a href="#">GO:0051547</a>	BP	regulation of keratinocyte migration	0	1	0.0103724
<a href="#">GO:0051549</a>	BP	positive regulation of keratinocyte migration	0	1	0.0103724
<a href="#">GO:0044283</a>	BP	small molecule biosynthetic process	1	2	0.0111576
<a href="#">GO:0021846</a>	BP	cell proliferation in forebrain	1	0	0.0111652
<a href="#">GO:0006633</a>	BP	fatty acid biosynthetic process	1	1	0.0115736
<a href="#">GO:0030574</a>	BP	collagen catabolic process	0	1	0.0117449
<a href="#">GO:0015820</a>	BP	leucine transport	0	1	0.0117529
<a href="#">GO:1900755</a>	BP	branched-chain amino-acid anion transport	0	1	0.0117529
<a href="#">GO:0051546</a>	BP	keratinocyte migration	0	1	0.0119144
<a href="#">GO:0044003</a>	BP	modification by symbiont of host morphology or physiology	0	1	0.013036
<a href="#">GO:0055057</a>	BP	neuroblast division	1	0	0.013864
<a href="#">GO:0015803</a>	BP	branched-chain aliphatic amino acid transport	0	1	0.0142855
<a href="#">GO:0035094</a>	BP	response to nicotine	0	1	0.0143034
<a href="#">GO:0044243</a>	BP	multicellular organismal catabolic process	0	1	0.0146319
<a href="#">GO:0042886</a>	BP	amide transport	1	0	0.015095
<a href="#">GO:0031915</a>	BP	positive regulation of synaptic plasticity	0	1	0.0165538
<a href="#">GO:0055093</a>	BP	response to hyperoxia	0	1	0.0168077
<a href="#">GO:0018195</a>	BP	peptidyl-arginine modification	0	1	0.0169921
<a href="#">GO:0006508</a>	BP	proteolysis	3	2	0.0178713
<a href="#">GO:0042493</a>	BP	response to drug	1	1	0.0179224
<a href="#">GO:0009065</a>	BP	glutamine family amino acid catabolic process	1	0	0.0185135
<a href="#">GO:0030858</a>	BP	positive regulation of epithelial cell differentiation	1	0	0.0194834
<a href="#">GO:0060033</a>	BP	anatomical structure regression	0	1	0.0198409
<a href="#">GO:0050775</a>	BP	positive regulation of dendrite morphogenesis	1	0	0.0198532
<a href="#">GO:0031668</a>	BP	cellular response to extracellular stimulus	1	1	0.0201539
<a href="#">GO:0021872</a>	BP	forebrain generation of neurons	1	0	0.0217616
<a href="#">GO:0060479</a>	BP	lung cell differentiation	1	0	0.0218822
<a href="#">GO:0060487</a>	BP	lung epithelial cell differentiation	1	0	0.0218822
<a href="#">GO:0008272</a>	BP	sulfate transport	1	0	0.0218896
<a href="#">GO:0008610</a>	BP	lipid biosynthetic process	2	1	0.022386
<a href="#">GO:0007566</a>	BP	embryo implantation	0	1	0.0232497
<a href="#">GO:0006525</a>	BP	arginine metabolic process	1	1	0.023798
<a href="#">GO:0007405</a>	BP	neuroblast proliferation	1	0	0.026249
<a href="#">GO:0048103</a>	BP	somatic stem cell division	1	0	0.0262981
<a href="#">GO:0072537</a>	BP	fibroblast activation	1	0	0.0271172
<a href="#">GO:0071496</a>	BP	cellular response to external stimulus	1	1	0.027315
<a href="#">GO:0051180</a>	BP	vitamin transport	1	0	0.0278874
<a href="#">GO:0016999</a>	BP	antibiotic metabolic process	1	0	0.0281423
<a href="#">GO:0034332</a>	BP	adherens junction organization	1	0	0.0283483
<a href="#">GO:0015804</a>	BP	neutral amino acid transport	0	1	0.0284833
<a href="#">GO:0051817</a>	BP	modification of morphology or physiology of other organism involved in symbiotic interaction	0	1	0.0287122
<a href="#">GO:0060428</a>	BP	lung epithelium development	1	0	0.0297913
<a href="#">GO:0050819</a>	BP	negative regulation of coagulation	0	1	0.0301457

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
GO:0035690	BP	cellular response to drug	1	0	0.0304062
GO:0017145	BP	stem cell division	1	0	0.031876
GO:0016051	BP	carbohydrate biosynthetic process	2	0	0.0325671
GO:0048545	BP	response to steroid hormone stimulus	0	2	0.0326385
GO:0006094	BP	gluconeogenesis	1	0	0.0327722
GO:0055114	BP	oxidation-reduction process	4	0	0.0349281
GO:0019048	BP	virus-host interaction	0	1	0.0359779
GO:0017144	BP	drug metabolic process	1	0	0.0366382
GO:0045746	BP	negative regulation of Notch signaling pathway	1	0	0.037303
GO:0016126	BP	sterol biosynthetic process	1	0	0.038073
GO:0006629	BP	lipid metabolic process	3	1	0.038336
GO:0006631	BP	fatty acid metabolic process	1	1	0.0387578
GO:0044419	BP	interspecies interaction between organisms	1	1	0.0398852
GO:0071347	BP	cellular response to interleukin-1	0	1	0.0403745
GO:0043648	BP	dicarboxylic acid metabolic process	1	0	0.0405356
GO:0032963	BP	collagen metabolic process	0	1	0.0411421
GO:0044259	BP	multicellular organismal macromolecule metabolic process	0	1	0.0411421
GO:0035821	BP	modification of morphology or physiology of other organism	0	1	0.0413052
GO:0043154	BP	negative regulation of cysteine-type endopeptidase activity involved in apoptotic process	1	0	0.0420778
GO:2000117	BP	negative regulation of cysteine-type endopeptidase activity	1	0	0.0420778
GO:0042398	BP	cellular modified amino acid biosynthetic process	0	1	0.0423695
GO:0006730	BP	one-carbon metabolic process	1	0	0.0425298
GO:0019319	BP	hexose biosynthetic process	1	0	0.0434838
GO:0030334	BP	regulation of cell migration	1	1	0.0435087
GO:0044236	BP	multicellular organismal metabolic process	0	1	0.0439448
GO:0061351	BP	neural precursor cell proliferation	1	0	0.0445523
GO:2000145	BP	regulation of cell motility	1	1	0.0461137
GO:0007586	BP	digestion	1	0	0.0463652
GO:0048814	BP	regulation of dendrite morphogenesis	1	0	0.0471453
GO:0070555	BP	response to interleukin-1	0	1	0.048985
GO:0034612	BP	response to tumor necrosis factor	0	1	0.0490052
GO:0019233	BP	sensory perception of pain	1	0	0.049195
GO:0032355	BP	response to estradiol stimulus	0	1	0.0499926
GO:0016020	CC	membrane	15	9	3.55E-05
GO:0005576	CC	extracellular region	6	4	0.000157129
GO:0005575	CC	cellular_component	30	8	0.000246254
GO:0044425	CC	membrane part	17	2	0.000315492
GO:0031224	CC	intrinsic to membrane	16	1	0.0004088
GO:0016021	CC	integral to membrane	15	1	0.000985323
GO:0017090	CC	meprin A complex	1	0	0.00188578
GO:0005615	CC	extracellular space	1	3	0.00527238
GO:0072562	CC	blood microparticle	0	1	0.00579968
GO:0072563	CC	endothelial microparticle	0	1	0.00579968
GO:0005886	CC	plasma membrane	8	3	0.00621419
GO:0071944	CC	cell periphery	8	3	0.0100907
GO:0044421	CC	extracellular region part	2	3	0.0113203
GO:0005624	CC	membrane fraction	3	0	0.0209092
GO:0005626	CC	insoluble fraction	3	0	0.0237271
GO:0019031	CC	viral envelope	1	0	0.0286916
GO:0000267	CC	cell fraction	3	0	0.035624
GO:0055036	CC	virion membrane	1	0	0.0422082
GO:0045177	CC	apical part of cell	2	0	0.0424893
GO:0030424	CC	axon	2	0	0.0442162
GO:0005811	CC	lipid particle	0	2	0.0461664
GO:0043034	CC	costamere	0	1	0.0479751

**Supplementary Table S1b.** Gene ontology enrichment test in the spleen of susceptible chicken line 7.2 with  $p < 0.05$  and  $\text{Log}_2$ -transformations of the normalization  $\geq 2$  (MF: molecular function, BP: biological process and CC: cellular component). The data showed the number of genes which were up- and downregulated in susceptible chicken line 7.2.

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
<a href="#">GO:0008933</a>	MF	lytic transglycosylase activity	0	1	0.0010512
<a href="#">GO:0022892</a>	MF	substrate-specific transporter activity	6	1	0.00105122
<a href="#">GO:0004055</a>	MF	argininosuccinate synthase activity	0	1	0.00213383
<a href="#">GO:0043825</a>	MF	succinylornithine transaminase activity	1	0	0.00273775
<a href="#">GO:0004026</a>	MF	alcohol O-acetyltransferase activity	0	1	0.00283308
<a href="#">GO:0034318</a>	MF	alcohol O-acyltransferase activity	0	1	0.00283308
<a href="#">GO:0034319</a>	MF	alcohol O-butanoyltransferase activity	0	1	0.00283308
<a href="#">GO:0034323</a>	MF	O-butanoyltransferase activity	0	1	0.00283308
<a href="#">GO:0034326</a>	MF	butanoyltransferase activity	0	1	0.00283308
<a href="#">GO:0034338</a>	MF	short-chain carboxylesterase activity	0	1	0.00283308
<a href="#">GO:0005215</a>	MF	transporter activity	6	1	0.0032377
<a href="#">GO:0005499</a>	MF	vitamin D binding	1	0	0.00362091
<a href="#">GO:0004611</a>	MF	phosphoenolpyruvate carboxykinase activity	1	0	0.00370373
<a href="#">GO:0004613</a>	MF	phosphoenolpyruvate carboxykinase (GTP) activity	1	0	0.00370373
<a href="#">GO:0008743</a>	MF	L-threonine 3-dehydrogenase activity	1	0	0.00371402
<a href="#">GO:0008508</a>	MF	bile acid:sodium symporter activity	1	0	0.00607798
<a href="#">GO:0008139</a>	MF	nuclear localization sequence binding	0	1	0.00648464
<a href="#">GO:0015204</a>	MF	urea transmembrane transporter activity	1	0	0.00665044
<a href="#">GO:0042887</a>	MF	amide transmembrane transporter activity	1	0	0.00665044
<a href="#">GO:0005184</a>	MF	neuropeptide hormone activity	1	0	0.00862614
<a href="#">GO:0015125</a>	MF	bile acid transmembrane transporter activity	1	0	0.0102939
<a href="#">GO:0003956</a>	MF	NAD(P)+-protein-arginine ADP-ribosyltransferase activity	0	1	0.0111821
<a href="#">GO:0015103</a>	MF	inorganic anion transmembrane transporter activity	2	0	0.011549
<a href="#">GO:0005344</a>	MF	oxygen transporter activity	1	0	0.0124526
<a href="#">GO:0022891</a>	MF	substrate-specific transmembrane transporter activity	5	0	0.012562
<a href="#">GO:0016740</a>	MF	transferase activity	2	7	0.01265
<a href="#">GO:0003918</a>	MF	DNA topoisomerase (ATP-hydrolyzing) activity	0	1	0.0134776
<a href="#">GO:0008553</a>	MF	hydrogen-exporting ATPase activity, phosphorylative mechanism	1	0	0.0148506
<a href="#">GO:0019825</a>	MF	oxygen binding	1	0	0.0180823
<a href="#">GO:0022857</a>	MF	transmembrane transporter activity	5	0	0.019283
<a href="#">GO:0008509</a>	MF	anion transmembrane transporter activity	2	0	0.0201608
<a href="#">GO:0003916</a>	MF	DNA topoisomerase activity	0	1	0.0219479
<a href="#">GO:0003810</a>	MF	protein-glutamine gamma-glutamyltransferase activity	0	1	0.0221803
<a href="#">GO:0022804</a>	MF	active transmembrane transporter activity	3	0	0.0225543
<a href="#">GO:0019842</a>	MF	vitamin binding	2	0	0.0236602
<a href="#">GO:0015116</a>	MF	sulfate transmembrane transporter activity	1	0	0.0238317
<a href="#">GO:0005048</a>	MF	signal sequence binding	0	1	0.0242385
<a href="#">GO:0004364</a>	MF	glutathione transferase activity	0	1	0.0244004
<a href="#">GO:0008009</a>	MF	chemokine activity	0	1	0.0266425
<a href="#">GO:0042379</a>	MF	chemokine receptor binding	0	1	0.0278065
<a href="#">GO:0016853</a>	MF	isomerase activity	1	1	0.0293523
<a href="#">GO:0016755</a>	MF	transferase activity, transferring amino-acyl groups	0	1	0.0297397
<a href="#">GO:0016413</a>	MF	O-acetyltransferase activity	0	1	0.0297724
<a href="#">GO:0008028</a>	MF	monocarboxylic acid transmembrane transporter activity	1	0	0.030432
<a href="#">GO:0015075</a>	MF	ion transmembrane transporter activity	4	0	0.0304919
<a href="#">GO:0015301</a>	MF	anion:anion antiporter activity	1	0	0.0381749
<a href="#">GO:0003824</a>	MF	catalytic activity	6	10	0.0387819
<a href="#">GO:0015291</a>	MF	secondary active transmembrane transporter activity	2	0	0.0397036
<a href="#">GO:0005343</a>	MF	organic acid:sodium symporter activity	1	0	0.0401934
<a href="#">GO:0016829</a>	MF	lyase activity	1	1	0.0415912
<a href="#">GO:0004181</a>	MF	metallocarboxypeptidase activity	1	0	0.0418653
<a href="#">GO:0008483</a>	MF	transaminase activity	1	0	0.0451902
<a href="#">GO:0004091</a>	MF	carboxylesterase activity	0	1	0.0467262
<a href="#">GO:0016831</a>	MF	carboxy-lyase activity	1	0	0.0488677
<a href="#">GO:0006525</a>	BP	arginine metabolic process	1	1	0.00025555
<a href="#">GO:0009308</a>	BP	amine metabolic process	2	3	0.00056722
<a href="#">GO:0016054</a>	BP	organic acid catabolic process	2	1	0.0010466
<a href="#">GO:0046395</a>	BP	carboxylic acid catabolic process	2	1	0.0010466

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
<a href="#">GO:0044282</a>	BP	small molecule catabolic process	2	1	0.00169233
<a href="#">GO:0044106</a>	BP	cellular amine metabolic process	2	2	0.00268388
<a href="#">GO:0009063</a>	BP	cellular amino acid catabolic process	2	0	0.00270262
<a href="#">GO:0009064</a>	BP	glutamine family amino acid metabolic process	1	1	0.00271965
<a href="#">GO:0051792</a>	BP	medium-chain fatty acid biosynthetic process	0	1	0.00283308
<a href="#">GO:0051793</a>	BP	medium-chain fatty acid catabolic process	0	1	0.00283308
<a href="#">GO:0006811</a>	BP	ion transport	5	1	0.00348546
<a href="#">GO:0006567</a>	BP	threonine catabolic process	1	0	0.00371402
<a href="#">GO:0019518</a>	BP	L-threonine catabolic process to glycine	1	0	0.00371402
<a href="#">GO:0006105</a>	BP	succinate metabolic process	1	0	0.00431246
<a href="#">GO:0019545</a>	BP	arginine catabolic process to succinate	1	0	0.00431246
<a href="#">GO:0009310</a>	BP	amine catabolic process	2	0	0.00439359
<a href="#">GO:0016360</a>	BP	sensory organ precursor cell fate determination	0	1	0.00504016
<a href="#">GO:0009068</a>	BP	aspartate family amino acid catabolic process	1	0	0.00521027
<a href="#">GO:0051791</a>	BP	medium-chain fatty acid metabolic process	0	1	0.00561711
<a href="#">GO:0048241</a>	BP	epinephrine transport	0	1	0.006018
<a href="#">GO:0048242</a>	BP	epinephrine secretion	0	1	0.006018
<a href="#">GO:0016338</a>	BP	calcium-independent cell-cell adhesion	0	1	0.00626024
<a href="#">GO:0071918</a>	BP	urea transmembrane transport	1	0	0.00665044
<a href="#">GO:0000270</a>	BP	peptidoglycan metabolic process	0	1	0.00773822
<a href="#">GO:0006566</a>	BP	threonine metabolic process	1	0	0.00831129
<a href="#">GO:0006527</a>	BP	arginine catabolic process	1	0	0.00895028
<a href="#">GO:0015840</a>	BP	urea transport	1	0	0.00906918
<a href="#">GO:0006607</a>	BP	NLS-bearing substrate import into nucleus	0	1	0.0106659
<a href="#">GO:0008052</a>	BP	sensory organ boundary specification	0	1	0.0107772
<a href="#">GO:0006526</a>	BP	arginine biosynthetic process	0	1	0.0124525
<a href="#">GO:0019752</a>	BP	carboxylic acid metabolic process	2	2	0.0124589
<a href="#">GO:0043436</a>	BP	oxoacid metabolic process	2	2	0.0124589
<a href="#">GO:0006082</a>	BP	organic acid metabolic process	2	2	0.0126423
<a href="#">GO:0006520</a>	BP	cellular amino acid metabolic process	2	1	0.013138
<a href="#">GO:0042180</a>	BP	cellular ketone metabolic process	2	2	0.013814
<a href="#">GO:0015698</a>	BP	inorganic anion transport	2	0	0.0140833
<a href="#">GO:0042886</a>	BP	amide transport	1	0	0.0146989
<a href="#">GO:0042415</a>	BP	norepinephrine metabolic process	0	1	0.0152179
<a href="#">GO:0015671</a>	BP	oxygen transport	1	0	0.0152386
<a href="#">GO:0015669</a>	BP	gas transport	1	0	0.0168414
<a href="#">GO:0009065</a>	BP	glutamine family amino acid catabolic process	1	0	0.0181944
<a href="#">GO:0030325</a>	BP	adrenal gland development	0	1	0.0182192
<a href="#">GO:0010160</a>	BP	formation of organ boundary	0	1	0.0206901
<a href="#">GO:0055010</a>	BP	ventricular cardiac muscle tissue morphogenesis	0	1	0.020926
<a href="#">GO:0048859</a>	BP	formation of anatomical boundary	0	1	0.02221
<a href="#">GO:0003229</a>	BP	ventricular cardiac muscle tissue development	0	1	0.02375
<a href="#">GO:0006471</a>	BP	protein ADP-ribosylation	0	1	0.0253868
<a href="#">GO:0008272</a>	BP	sulfate transport	1	0	0.0267008
<a href="#">GO:0006584</a>	BP	catecholamine metabolic process	0	1	0.0274192
<a href="#">GO:0006094</a>	BP	gluconeogenesis	1	0	0.0274712
<a href="#">GO:0006265</a>	BP	DNA topological change	0	1	0.0284711
<a href="#">GO:0009712</a>	BP	catechol-containing compound metabolic process	0	1	0.0287056
<a href="#">GO:0006820</a>	BP	anion transport	2	0	0.0288136
<a href="#">GO:0071705</a>	BP	nitrogen compound transport	1	1	0.0297978
<a href="#">GO:0050432</a>	BP	catecholamine secretion	0	1	0.0303896
<a href="#">GO:0072537</a>	BP	fibroblast activation	1	0	0.0305875
<a href="#">GO:0034311</a>	BP	diol metabolic process	0	1	0.0315112
<a href="#">GO:0003208</a>	BP	cardiac ventricle morphogenesis	0	1	0.0348399
<a href="#">GO:0019319</a>	BP	hexose biosynthetic process	1	0	0.0363584
<a href="#">GO:0009084</a>	BP	glutamine family amino acid biosynthetic process	0	1	0.0364427
<a href="#">GO:0018149</a>	BP	peptide cross-linking	0	1	0.0376767
<a href="#">GO:0055008</a>	BP	cardiac muscle tissue morphogenesis	0	1	0.0381418
<a href="#">GO:0051937</a>	BP	catecholamine transport	0	1	0.0383056

ACC	Category	Definition	Regulated gene		p-value
			Up	Down	
<a href="#">GO:0006810</a>	BP	transport	7	3	0.0403819
<a href="#">GO:0043648</a>	BP	dicarboxylic acid metabolic process	1	0	0.0408411
<a href="#">GO:0035270</a>	BP	endocrine system development	0	1	0.0424684
<a href="#">GO:0018958</a>	BP	phenol-containing compound metabolic process	0	1	0.0442745
<a href="#">GO:0051234</a>	BP	establishment of localization	7	3	0.0451024
<a href="#">GO:0006313</a>	BP	transposition, DNA-mediated	0	1	0.0489602
<a href="#">GO:0060415</a>	BP	muscle tissue morphogenesis	0	1	0.0498833
<a href="#">GO:0005811</a>	CC	lipid particle	0	2	0.00111071
<a href="#">GO:0031225</a>	CC	anchored to membrane	0	2	0.0064666
<a href="#">GO:0070701</a>	CC	mucus layer	0	1	0.00906814
<a href="#">GO:0070702</a>	CC	inner mucus layer	0	1	0.00906814
<a href="#">GO:0070703</a>	CC	outer mucus layer	0	1	0.00906814
<a href="#">GO:0005833</a>	CC	hemoglobin complex	1	0	0.0103916
<a href="#">GO:0016471</a>	CC	vacuolar proton-transporting V-type ATPase complex	1	0	0.0159078
<a href="#">GO:0005865</a>	CC	striated muscle thin filament	0	1	0.0190633
<a href="#">GO:0016020</a>	CC	membrane	9	9	0.0205417
<a href="#">GO:0033176</a>	CC	proton-transporting V-type ATPase complex	1	0	0.025971

**Supplementary Table S1c.** Gene ontology enrichment test of resistant line 6.3 versus susceptible line 7.2 in the spleen with  $p < 0.05$  and Log2-transformations of the normalization of resistant/susceptible  $\geq 2$  (MF: molecular function, BP: biological process and CC: cellular component). The data showed the number of genes which were up- and downregulated in resistant chicken line 6.3 compared to susceptible chicken line 7.2.

ACC	Category	Definition	Regulated genes		p-value
			Up	Down	
<a href="#">GO:0004175</a>	MF	endopeptidase activity	2	2	7.41E-05
<a href="#">GO:0047429</a>	MF	nucleoside-triphosphate diphosphatase activity	1	0	0.000534732
<a href="#">GO:0070011</a>	MF	peptidase activity, acting on L-amino acid peptides	6	2	0.000766021
<a href="#">GO:0004533</a>	MF	exoribonuclease H activity	1	1	0.000845852
<a href="#">GO:0008233</a>	MF	peptidase activity	6	2	0.000892198
<a href="#">GO:0004527</a>	MF	exonuclease activity	2	1	0.00159076
<a href="#">GO:0051786</a>	MF	all-trans-retinol 13,14-reductase activity	1	0	0.00182499
<a href="#">GO:0008933</a>	MF	lytic transglycosylase activity	0	1	0.00219589
<a href="#">GO:0016829</a>	MF	lyase activity	3	1	0.0023682
<a href="#">GO:0015563</a>	MF	uptake transmembrane transporter activity	1	0	0.00318461
<a href="#">GO:0080138</a>	MF	borate uptake transmembrane transporter activity	1	0	0.00318461
<a href="#">GO:0052582</a>	MF	(+)-menthofuran synthase activity	1	0	0.00352433
<a href="#">GO:0004532</a>	MF	exoribonuclease activity	1	1	0.00356907
<a href="#">GO:0016896</a>	MF	exoribonuclease activity, producing 5'-phosphomonoesters	1	1	0.00356907
<a href="#">GO:0016796</a>	MF	exonuclease activity, active with either ribo- or deoxyribonucleic acids and producing 5'-phosphomonoesters	1	1	0.00388849
<a href="#">GO:0004518</a>	MF	nuclease activity	2	3	0.00421236
<a href="#">GO:0004222</a>	MF	metalloendopeptidase activity	2	1	0.00452514
<a href="#">GO:0031694</a>	MF	alpha-2A adrenergic receptor binding	0	1	0.00562692
<a href="#">GO:0003964</a>	MF	RNA-directed DNA polymerase activity	1	3	0.00598317
<a href="#">GO:0004611</a>	MF	phosphoenolpyruvate carboxykinase activity	1	0	0.00614515
<a href="#">GO:0004613</a>	MF	phosphoenolpyruvate carboxykinase (GTP) activity	1	0	0.00614515
<a href="#">GO:0015105</a>	MF	arsenite transmembrane transporter activity	1	0	0.00696569
<a href="#">GO:0004566</a>	MF	beta-glucuronidase activity	1	0	0.0073504
<a href="#">GO:0004523</a>	MF	ribonuclease H activity	1	2	0.00751456
<a href="#">GO:0047547</a>	MF	2-methylcitrate dehydratase activity	0	1	0.00789084
<a href="#">GO:0034061</a>	MF	DNA polymerase activity	1	3	0.00853451
<a href="#">GO:0001733</a>	MF	galactosylceramide sulfotransferase activity	0	1	0.00873618
<a href="#">GO:0050694</a>	MF	galactose 3-O-sulfotransferase activity	0	1	0.00873618
<a href="#">GO:0015370</a>	MF	solute:sodium symporter activity	0	2	0.00904613



ACC	Category	Definition	Regulated genes		p-value
			Up	Down	
GO:0016836	MF	hydro-lyase activity	2	0	0.00949916
GO:0004190	MF	aspartic-type endopeptidase activity	1	2	0.00975985
GO:0070001	MF	aspartic-type peptidase activity	1	2	0.00975985
GO:0035529	MF	NADH pyrophosphatase activity	1	0	0.0100091
GO:0046715	MF	borate transmembrane transporter activity	1	0	0.0100095
GO:0016891	MF	endoribonuclease activity, producing 5'-phosphomonoesters	1	2	0.0101006
GO:0015168	MF	glycerol transmembrane transporter activity	1	0	0.0103365
GO:0004519	MF	endonuclease activity	3	1	0.010481
GO:0015204	MF	urea transmembrane transporter activity	1	0	0.0109939
GO:0042887	MF	amide transmembrane transporter activity	1	0	0.0109939
GO:0004668	MF	protein-arginine deiminase activity	0	1	0.0110373
GO:0008508	MF	bile acid:sodium symporter activity	1	0	0.0110595
GO:0016893	MF	endonuclease activity, active with either ribo- or deoxyribonucleic acids and producing 5'-phosphomonoesters	1	2	0.0113342
GO:0005355	MF	glucose transmembrane transporter activity	0	1	0.0119593
GO:0015145	MF	monosaccharide transmembrane transporter activity	0	1	0.0119593
GO:0015149	MF	hexose transmembrane transporter activity	0	1	0.0119593
GO:0004521	MF	endoribonuclease activity	1	2	0.013506
GO:0003858	MF	3-hydroxybutyrate dehydrogenase activity	1	0	0.0143252
GO:0016835	MF	carbon-oxygen lyase activity	2	0	0.0144079
GO:0016491	MF	oxidoreductase activity	6	0	0.0145508
GO:0004170	MF	dUTP diphosphatase activity	0	1	0.0151129
GO:0003824	MF	catalytic activity	16	10	0.0155904
GO:0004540	MF	ribonuclease activity	1	2	0.0177235
GO:0004528	MF	phosphodiesterase I activity	1	0	0.0179027
GO:0015125	MF	bile acid transmembrane transporter activity	1	0	0.0181056
GO:0015166	MF	polyol transmembrane transporter activity	1	0	0.0182634
GO:0008237	MF	metallopeptidase activity	3	1	0.0184625
GO:0015294	MF	solute:cation symporter activity	0	2	0.0189906
GO:0008242	MF	omega peptidase activity	0	1	0.0199636
GO:0001968	MF	fibronectin binding	0	1	0.0201884
GO:0043169	MF	cation binding	14	4	0.0206679
GO:0043167	MF	ion binding	14	4	0.0209605
GO:0015665	MF	alcohol transmembrane transporter activity	1	0	0.0216736
GO:0016779	MF	nucleotidyltransferase activity	1	3	0.0231699
GO:0004497	MF	monooxygenase activity	2	0	0.0252525
GO:0016813	MF	hydrolase activity, acting on carbon-nitrogen	0	1	0.0269252
GO:0004551	MF	nucleotide diphosphatase activity	1	0	0.0270368
GO:0031690	MF	adrenergic receptor binding	0	1	0.0288964
GO:0046872	MF	metal ion binding	13	4	0.0361807
GO:0015081	MF	sodium ion transmembrane transporter activity	0	2	0.0377544
GO:0016787	MF	hydrolase activity	9	4	0.0384575
GO:0051119	MF	sugar transmembrane transporter activity	0	1	0.0436929
GO:0004089	MF	carbonate dehydratase activity	2	0	0.0445549
GO:0015293	MF	symporter activity	0	2	0.0478865
GO:0004866	MF	endopeptidase inhibitor activity	2	0	0.0482536
GO:0061135	MF	endopeptidase regulator activity	2	0	0.0490373
GO:0008028	MF	monocarboxylic acid transmembrane transporter activity	1	0	0.0499747
GO:0044419	BP	interspecies interaction between organisms	1	1	2.12E-05
GO:0030574	BP	collagen catabolic process	0	2	0.000172781
GO:0044243	BP	multicellular organismal catabolic process	0	2	0.000244847
GO:0006720	BP	isoprenoid metabolic process	3	0	0.000529324
GO:0007566	BP	embryo implantation	1	1	0.000690813
GO:0016032	BP	viral reproduction	1	3	0.000938757
GO:0043627	BP	response to estrogen stimulus	0	2	0.0011929
GO:0051704	BP	multi-organism process	1	6	0.00171616
GO:0032963	BP	collagen metabolic process	1	1	0.00227394
GO:0044259	BP	multicellular organismal macromolecule metabolic process	1	1	0.00227394
GO:0044236	BP	multicellular organismal metabolic process	0	2	0.00250464

ACC	Category	Definition	Regulated genes		p-value
			Up	Down	
GO:0046080	BP	dUTP metabolic process	0	2	0.00262305
GO:0007584	BP	response to nutrient	1	2	0.00263182
GO:0009211	BP	pyrimidine deoxyribonucleoside triphosphate metabolic process	0	2	0.0028462
GO:0009219	BP	pyrimidine deoxyribonucleotide metabolic process	0	2	0.00304728
GO:0009200	BP	deoxyribonucleoside triphosphate metabolic process	0	2	0.00352186
GO:0032355	BP	response to estradiol stimulus	0	2	0.00371478
GO:0019629	BP	propionate catabolic process, 2-methylcitrate cycle	0	1	0.00400373
GO:0009394	BP	2'-deoxyribonucleotide metabolic process	0	2	0.0040798
GO:0006721	BP	terpenoid metabolic process	2	0	0.00411059
GO:0015850	BP	organic alcohol transport	1	1	0.00445688
GO:0045471	BP	response to ethanol	1	1	0.00455246
GO:0097305	BP	response to alcohol	1	1	0.00455246
GO:0051701	BP	interaction with host	1	1	0.00491978
GO:0007565	BP	female pregnancy	0	2	0.0049753
GO:0009262	BP	deoxyribonucleotide metabolic process	0	2	0.00503283
GO:0008299	BP	isoprenoid biosynthetic process	2	0	0.00590401
GO:0006508	BP	proteolysis	6	2	0.00592331
GO:0031667	BP	response to nutrient levels	2	2	0.00599592
GO:0080029	BP	cellular response to boron-containing substance levels	1	0	0.00603303
GO:0001955	BP	blood vessel maturation	0	1	0.0063067
GO:0006278	BP	RNA-dependent DNA replication	1	3	0.00643116
GO:0009147	BP	pyrimidine nucleoside triphosphate metabolic process	0	2	0.00656845
GO:0019896	BP	axon transport of mitochondrion	0	1	0.00687467
GO:0015700	BP	arsenite transport	1	0	0.00696569
GO:0032526	BP	response to retinoic acid	0	2	0.00714133
GO:0035445	BP	borate transmembrane transport	1	0	0.00717238
GO:0019087	BP	transformation of host cell by virus	0	1	0.00723965
GO:0009991	BP	response to extracellular stimulus	2	2	0.00729875
GO:0019541	BP	propionate metabolic process	0	1	0.00789084
GO:0019543	BP	propionate catabolic process	0	1	0.00789084
GO:0033189	BP	response to vitamin A	0	2	0.00804444
GO:0009719	BP	response to endogenous stimulus	1	4	0.00995205
GO:0010036	BP	response to boron-containing substance	1	0	0.0100095
GO:0046713	BP	borate transport	1	0	0.0100095
GO:0071705	BP	nitrogen compound transport	2	1	0.0101633
GO:0048241	BP	epinephrine transport	0	1	0.0102815
GO:0048242	BP	epinephrine secretion	0	1	0.0102815
GO:0044403	BP	symbiosis, encompassing mutualism through parasitism	1	1	0.0105244
GO:0015816	BP	glycine transport	0	1	0.0108562
GO:0051385	BP	response to mineralocorticoid stimulus	1	0	0.0109053
GO:0051412	BP	response to corticosterone stimulus	1	0	0.0109053
GO:0015793	BP	glycerol transport	1	0	0.0109934
GO:0071918	BP	urea transmembrane transport	1	0	0.0109939
GO:0000052	BP	citrulline metabolic process	0	1	0.0110373
GO:0018101	BP	peptidyl-citrulline biosynthetic process from peptidyl-arginine	0	1	0.0110373
GO:0019240	BP	citrulline biosynthetic process	0	1	0.0110373
GO:0071460	BP	cellular response to cell-matrix adhesion	0	1	0.0111982
GO:0071404	BP	cellular response to low-density lipoprotein particle stimulus	0	1	0.0112234
GO:0015074	BP	DNA integration	1	2	0.0119014
GO:0006220	BP	pyrimidine nucleotide metabolic process	0	2	0.0121271
GO:0042572	BP	retinol metabolic process	1	0	0.0125948
GO:0032328	BP	alanine transport	0	1	0.0126352
GO:0048545	BP	response to steroid hormone stimulus	1	2	0.0138253
GO:0033273	BP	response to vitamin	0	2	0.0142373
GO:0000270	BP	peptidoglycan metabolic process	0	1	0.0144731
GO:0071402	BP	cellular response to lipoprotein particle stimulus	0	1	0.0151801
GO:0055098	BP	response to low-density lipoprotein particle stimulus	0	1	0.0151914
GO:0072527	BP	pyrimidine-containing compound metabolic process	0	2	0.0157354
GO:0015840	BP	urea transport	1	0	0.0165188

ACC	Category	Definition	Regulated genes		p-value
			Up	Down	
GO:0015824	BP	proline transport	0	1	0.0180736
GO:0019047	BP	provirus integration	1	0	0.0181211
GO:0019061	BP	uncoating of virus	1	0	0.0181211
GO:0030069	BP	lysogeny	1	0	0.0181211
GO:0060346	BP	bone trabecula formation	0	1	0.0187984
GO:0061430	BP	bone trabecula morphogenesis	0	1	0.0187984
GO:0009725	BP	response to hormone stimulus	2	2	0.0189292
GO:0090305	BP	nucleic acid phosphodiester bond hydrolysis	1	3	0.0189859
GO:0055094	BP	response to lipoprotein stimulus	0	1	0.0191323
GO:0071702	BP	organic substance transport	1	3	0.01926
GO:0051547	BP	regulation of keratinocyte migration	0	1	0.0193231
GO:0051549	BP	positive regulation of keratinocyte migration	0	1	0.0193231
GO:0051546	BP	keratinocyte migration	0	1	0.0217672
GO:0022415	BP	viral reproductive process	1	1	0.0220443
GO:0055114	BP	oxidation-reduction process	6	0	0.0224917
GO:0008643	BP	carbohydrate transport	1	1	0.0228045
GO:0015820	BP	leucine transport	0	1	0.0231931
GO:1900755	BP	branched-chain amino-acid anion transport	0	1	0.0231931
GO:0001957	BP	intramembranous ossification	0	1	0.0234858
GO:0036072	BP	direct ossification	0	1	0.0234858
GO:0032868	BP	response to insulin stimulus	1	1	0.0246032
GO:0042415	BP	norepinephrine metabolic process	0	1	0.0251005
GO:0006776	BP	vitamin A metabolic process	1	0	0.0255507
GO:0044003	BP	modification by symbiont of host morphology or physiology	0	1	0.0259203
GO:0007412	BP	axon target recognition	0	1	0.0259526
GO:0060612	BP	adipose tissue development	1	0	0.0264902
GO:0001666	BP	response to hypoxia	0	2	0.0267097
GO:0015803	BP	branched-chain aliphatic amino acid transport	0	1	0.0271136
GO:0019059	BP	initiation of viral infection	1	0	0.0271628
GO:0030260	BP	entry into host cell	1	0	0.0271628
GO:0044409	BP	entry into host	1	0	0.0271628
GO:0051806	BP	entry into cell of other organism involved in symbiotic interaction	1	0	0.0271628
GO:0051828	BP	entry into other organism involved in symbiotic interaction	1	0	0.0271628
GO:0042886	BP	amide transport	1	0	0.0273651
GO:0055093	BP	response to hyperoxia	0	1	0.0277426
GO:0046685	BP	response to arsenic-containing substance	1	0	0.027967
GO:0035094	BP	response to nicotine	0	1	0.0285816
GO:0015791	BP	polyol transport	1	0	0.0298649
GO:0031915	BP	positive regulation of synaptic plasticity	0	1	0.0301821
GO:0001523	BP	retinoid metabolic process	1	0	0.0305911
GO:0070482	BP	response to oxygen levels	0	2	0.0321618
GO:0019069	BP	viral capsid assembly	1	0	0.0325204
GO:0046797	BP	viral procapsid maturation	1	0	0.0325204
GO:0060325	BP	face morphogenesis	0	1	0.0325838
GO:0060416	BP	response to growth hormone stimulus	1	0	0.0327757
GO:0016101	BP	diterpenoid metabolic process	1	0	0.0328931
GO:0030325	BP	adrenal gland development	0	1	0.0328938
GO:0018195	BP	peptidyl-arginine modification	0	1	0.0333781
GO:0060343	BP	trabecula formation	0	1	0.0334187
GO:0060033	BP	anatomical structure regression	0	1	0.0346531
GO:0060323	BP	head morphogenesis	0	1	0.0351934
GO:0046627	BP	negative regulation of insulin receptor signaling pathway	0	1	0.0353221
GO:1900077	BP	negative regulation of cellular response to insulin stimulus	0	1	0.0353221
GO:0055010	BP	ventricular cardiac muscle tissue morphogenesis	0	1	0.0364566
GO:0043434	BP	response to peptide hormone stimulus	1	1	0.0372623
GO:0046626	BP	regulation of insulin receptor signaling pathway	0	1	0.0388746
GO:1900076	BP	regulation of cellular response to insulin stimulus	0	1	0.0388746
GO:0003229	BP	ventricular cardiac muscle tissue development	0	1	0.0403232
GO:0060324	BP	face development	0	1	0.0410943

ACC	Category	Definition	Regulated genes		p-value
			Up	Down	
<a href="#">GO:0052126</a>	BP	movement in host environment	1	0	0.0413725
<a href="#">GO:0052192</a>	BP	movement in environment of other organism	1	0	0.0413725
<a href="#">GO:0021700</a>	BP	developmental maturation	1	1	0.042601
<a href="#">GO:0007628</a>	BP	adult walking behavior	0	1	0.0432687
<a href="#">GO:0006584</a>	BP	catecholamine metabolic process	0	1	0.0455282
<a href="#">GO:0006260</a>	BP	DNA replication	1	3	0.0473241
<a href="#">GO:0061383</a>	BP	trabecula morphogenesis	0	1	0.047444
<a href="#">GO:0042493</a>	BP	response to drug	1	1	0.0481178
<a href="#">GO:0042755</a>	BP	eating behavior	0	1	0.0481504
<a href="#">GO:0015804</a>	BP	neutral amino acid transport	0	1	0.0483029
<a href="#">GO:0009712</a>	BP	catechol-containing compound metabolic process	0	1	0.0484574
<a href="#">GO:0050432</a>	BP	catecholamine secretion	0	1	0.049897
<a href="#">GO:0044423</a>	CC	virion part	2	3	2.65E-05
<a href="#">GO:0020002</a>	CC	host cell plasma membrane	1	3	5.48E-05
<a href="#">GO:0055036</a>	CC	virion membrane	1	0	5.77E-05
<a href="#">GO:0033644</a>	CC	host cell membrane	1	3	7.41E-05
<a href="#">GO:0044218</a>	CC	other organism cell membrane	1	3	7.92E-05
<a href="#">GO:0044279</a>	CC	other organism membrane	1	3	7.92E-05
<a href="#">GO:0019012</a>	CC	virion	1	4	8.63E-05
<a href="#">GO:0018995</a>	CC	host	1	3	0.000268057
<a href="#">GO:0033643</a>	CC	host cell part	1	3	0.000268057
<a href="#">GO:0043657</a>	CC	host cell	1	3	0.000268057
<a href="#">GO:0043245</a>	CC	extraorganismal space	1	3	0.000280882
<a href="#">GO:0044215</a>	CC	other organism	1	3	0.000280882
<a href="#">GO:0044216</a>	CC	other organism cell	1	3	0.000280882
<a href="#">GO:0044217</a>	CC	other organism part	1	3	0.000280882
<a href="#">GO:0005576</a>	CC	extracellular region	8	4	0.00111473
<a href="#">GO:0031225</a>	CC	anchored to membrane	1	2	0.00119462
<a href="#">GO:0044421</a>	CC	extracellular region part	5	3	0.00261723
<a href="#">GO:0005811</a>	CC	lipid particle	0	2	0.00316573
<a href="#">GO:0071575</a>	CC	integral to external side of plasma membrane	0	1	0.00385823
<a href="#">GO:0016020</a>	CC	membrane	21	9	0.00416239
<a href="#">GO:0016590</a>	CC	ACF complex	0	1	0.0104395
<a href="#">GO:0031224</a>	CC	intrinsic to membrane	21	0	0.0112493
<a href="#">GO:0032588</a>	CC	trans-Golgi network membrane	0	1	0.0118958
<a href="#">GO:0005678</a>	CC	chromatin assembly complex	0	1	0.0143956
<a href="#">GO:0031233</a>	CC	intrinsic to external side of plasma membrane	0	1	0.0206332
<a href="#">GO:0005578</a>	CC	proteinaceous extracellular matrix	0	4	0.02211
<a href="#">GO:0019028</a>	CC	viral capsid	1	1	0.0306338
<a href="#">GO:0071944</a>	CC	cell periphery	12	3	0.0307419
<a href="#">GO:0044425</a>	CC	membrane part	20	2	0.0316867
<a href="#">GO:0031012</a>	CC	extracellular matrix	0	4	0.0324155
<a href="#">GO:0016021</a>	CC	integral to membrane	18	1	0.0337337
<a href="#">GO:0005886</a>	CC	plasma membrane	11	3	0.0374987
<a href="#">GO:0005887</a>	CC	integral to plasma membrane	0	4	0.0433339
<a href="#">GO:0019031</a>	CC	viral envelope	1	0	0.047653

**Supplementary Table S2.** Details of the 107 novel up- and downregulated genes in the spleen of the two chicken lines. The data showed significant changes in the gene expression of the 107 novel genes in the NE-afflicted chicken lines. The genes included here showed significant differences in gene expression ( $p < 0.001$ , Log<sub>2</sub>-transformations of the normalization).

Align	ID	Line 6.3	Line 7.2	P-Value	Align	ID	Line 6.3	Line 7.2	P-Value
1	MERGE000551	2136.97	0.299379	0.00001	55	MERGE026303	722.45	0.911791	0.000069
2	MERGE000617	5.35256	0.0971332	0.00003	56	MERGE026452	0.691953	23.303	0.000232
3	MERGE000618	3.50802	0.188697	0.000026	57	MERGE026502	17.3414	2.29048	0.000194
4	MERGE000944	0.131426	3.34162	0.000013	58	MERGE026554	0.498798	17.4815	0.00029
5	MERGE001890	33.1856	2.09431	0.000024	59	MERGE026559	56.695	1.21542	0.000011
6	MERGE001892	1.94946	0.0565148	0.000002	60	MERGE026611	0.00466288	0.358285	0.000037
7	MERGE001986	1.62426	0.0174069	0.000223	61	MERGE026690	0	150808	0.000169
8	MERGE003380	2.36542	1.09E-08	0.00002	62	MERGE026742	17.7466	0.111535	0.000002
9	MERGE004114	2542.29	418.361	0.00012	63	MERGE026743	12.0938	0.296218	0.000017
10	MERGE004703	27.5891	8.14928	0.000052	64	MERGE026977	0.0841445	6.22033	0.000089
11	MERGE006359	0.347298	4.20567	0.000181	65	MERGE027165	7.39997	0.373603	0.000195
12	MERGE006582	0.0887352	2.36354	0.000212	66	MERGE027183	516.88	0.427449	0.000209
13	MERGE006584	0.0960111	3.63323	0.00003	67	MERGE027402	0.166846	9.39216	0.000047
14	MERGE006615	203.441	4.1005	0.00048	68	MERGE027408	0.116773	9.01353	0.000007
15	MERGE007249	1807.33	131.641	0.00028	69	MERGE027425	31.3806	3.20114	0.000269
16	MERGE007250	3656.99	370.669	0.00024	70	MERGE027438	52.4236	1.53551	0.000097
17	MERGE008766	0.115329	645.198	0.000005	71	MERGE027503	0.506263	14.3587	0.000001
18	MERGE009685	135.27	11.3463	0.000248	72	MERGE027638	28.9093	4.60078	0.000003
19	MERGE009859	0.0158767	1.66938	0.00013	73	MERGE027776	3.48675	29.1998	0.000005
20	MERGE009862	0.0147668	1.11988	0.000079	74	MERGE027843	0.265967	3.62531	0.000127
21	MERGE011093	0.260391	9.21101	0.000079	75	MERGE027851	9.92577	1.11266	0.000149
22	MERGE011720	0.0939934	2.42406	0.000163	76	MERGE027864	5.03866	0.0589511	0.000035
23	MERGE011796	1.17005	9.83704	0.000165	77	MERGE027951	0.424828	14.1378	0.000013
24	MERGE011843	189.587	38.0563	0.00063	78	MERGE028014	0.140447	4.5427	0.000004
25	MERGE012002	5.91058	0.0707595	0.000001	79	MERGE028162	45.366	3.25828	0.000108
26	MERGE012743	101.042	21.7745	0.000063	80	MERGE028374	1.14716	21.675	0.000001
27	MERGE012902	1.52806	0.0779027	0.000103	81	MERGE028465	31.9067	0.121619	0.000022
28	MERGE013363	42.4419	11.5543	0.000001	82	MERGE028470	34.982	3.54287	0.000052
29	MERGE014107	14.2182	0.0221362	0.000022	83	MERGE028475	30.2852	0.441379	0.000004
30	MERGE014878	94.7909	26.3151	0.000002	84	MERGE028484	0.0788914	2.33215	0.000108
31	MERGE016657	0.210053	0.010179	0.000263	85	MERGE028525	0.314738	5.959	0.000095
32	MERGE016754	1.9062	0.201944	0.000114	86	MERGE028547	0.0387693	3.16784	0.000089
33	MERGE017199	3.5207	0.160044	0.000011	87	MERGE028556	0.168418	12.3046	0.00008
34	MERGE017201	3.94706	0.199663	0.00018	88	MERGE028770	11.7212	0.434151	0.000083
35	MERGE017202	2.71074	0.0834113	0.00001	89	MERGE028908	824.188	2388.62	0.000042
36	MERGE017811	51.1047	0.968184	0.000002	90	MERGE028967	8.73409	0.203217	0.000003
37	MERGE017813	127.141	6.51689	0.000004	91	MERGE028983	0.00234716	3.17869	0.000269
38	MERGE018593	7.47913	0.624983	0.000105	92	MERGE029032	0.49295	15.8866	0.000007
39	MERGE019909	22.6466	3.91193	0.000001	93	MERGE029081	0.012317	4.0843	0.0001
40	MERGE023028	17.0676	0.651791	0.000001	94	MERGE029100	13.0374	0.319954	0.00018
41	MERGE023671	41.0883	6.09047	0.000039	95	MERGE029165	15.0278	436.474	0.00008
42	MERGE025414	2.48584	0.0616675	0.000194	96	MERGE029168	209.505	1467.47	0.00010
43	MERGE025515	4.8911	0.211326	0.000001	97	MERGE029220	3.30095	0.0202832	0.000002
44	MERGE025584	8.08979	0.0975418	0.000009	98	MERGE029362	7.7485	0.033152	0.000121
45	MERGE025588	6.15473	0.169144	0.000098	99	MERGE029392	0.208215	34.6643	0.000002
46	MERGE025594	6.4614	0.0935933	0.00004	100	MERGE029474	6.33528	0.0620386	0.000001
47	MERGE025619	5.55924	0.0589723	0.000007	101	MERGE029569	7.9446	0.216283	0.000048
48	MERGE025745	1.19203	12.2097	0.000055	102	MERGE029570	6.57315	0.252599	0.000038

<b>Align</b>	<b>ID</b>	<b>Line 6.3</b>	<b>Line 7.2</b>	<b>P-Value</b>	<b>Align</b>	<b>ID</b>	<b>Line 6.3</b>	<b>Line 7.2</b>	<b>P-Value</b>
49	MERGEG025809	44.6485	0.794799	0.00001	103	MERGEG029610	7.61695	69.81	0.000166
50	MERGEG025958	3.13714	4.03167	0.000011	104	MERGEG029676	37.4481	1.32459	0.000046
51	MERGEG025992	320.944	0.0198383	0.000031	105	MERGEG029773	7.31126	0.131129	0.000256
52	MERGEG026053	9.61143	0.479531	0.000164	106	MERGEG029791	25.0124	3.28569	0.000117
53	MERGEG026071	105.14	29.9747	0.000108	107	MERGEG030130	31.3201	493.883	0.00026
54	MERGEG026263	102.943	15.0452	0.000001					

**Supplementary Table S3.** Differentially expressed genes related to antigen processing between the spleen of each of the samples and the two chicken lines. This data showed significant changes in the gene expression of the 139 immune-related genes in the two NE-afflicted chicken lines. The genes included here showed significant differences in gene expression with  $p < 0.01$ , Log<sub>2</sub>-transformations of the normalization.

Gene name	Accession no	Fold changes	
		Line 6.3	Line 7.2
Beta-defensin 1 (AvBD1) gene	NM_204993	6.27	3.09
Beta-defensin 3 ST1 (AvBD3ST1) gene	XM_004934447	-1.73	-0.82
Beta-defensin 3 ST2 (AvBD3ST2) gene	NM_001277431	-1.19	-1.38
Beta-defensin 9 (AvBD9) gene	AY621321	7.01	7.04
Beta-defensin 7 (AvBD7) gene	AY621322	5.68	0.00
Beta-defensin 10 (AvBD10) gene	AY621323	0	0
Bundling protein	NM_204127	8.38	8.18
Rho GDP dissociation inhibitor (GDI) beta	NM_001277364	7.73	7.71
Actin related protein 2/3 complex, subunit 1B	NM_001030632	8.82	8.75
Brain abundant, membrane attached signal protein 1	NM_204116	7.99	8.29
Beaded filament structural protein 1	NM_205151	3.87	2.77
Chromosome 6 open reading frame	XM_001231980	6.68	6.48
Complement component 1, q subcomponent, A chain	XM_417654	7.66	8.00
Complement component 1, q subcomponent, C chain	XM_417653	6.57	6.86
Coiled-coil domain containing 57	XM_415635	-3.32	9.33
CD3e molecule, epsilon	NM_206904	8.48	8.80
Immunoglobulin-associated beta	NM_001006328	7.06	7.14
Carbohydrate (N-acetylglucosamine-6-O)sulfotransferase 2	XM_003641759	6.27	6.96
Cold inducible RNA binding protein	NM_001031347	8.97	9.30
CKLF-like MARVEL transmembrane domain containing 3	NM_001001778	7.52	7.99
Complement component (3d/Epstein Barr virus) receptor 2	XM_002196472	6.87	6.10
Cellular repressor of E1A-stimulated genes 1	XM_003640464	8.70	8.19
Colony stimulating factor 3 receptor	NM_001030898	7.43	6.99
C-src tyrosine kinase	NM_205425	10.16	9.96
Cytochrome b-245, beta polypeptide	NM_001100286	6.73	7.17
Cytohesin 1	NM_001031105	7.61	7.95
Dual adaptor of phosphotyrosine and 3-phosphoinositides	NM_001012933	6.04	6.08
Deleted in malignant brain tumors 1	XM_003643135.1	6.23	6.22
Ets variant gene 6	NM_001199273	7.46	0.00
Extracellular fatty acid binding protein	AY545055	8.36	8.14
Formin-like 1	XM_001234504	8.03	8.05
Guanine nucleotide binding protein	NM_205402	8.18	8.09
GRB2-related adaptor protein	NM_001277553	7.20	7.61
Alpha-D-globin	NM_001004375	10.82	7.04
Hepatic and glial cell adhesion molecule	XM_425793	7.92	6.70
HtrA serine peptidase 1	XM_003641501	6.00	5.92
Hydrogen voltage-gated channel 1	NM_001030663	7.08	7.40
Interferon, gamma-inducible protein 30	XM_418246	8.61	8.86
Immunoglobulin J polypeptide	NM_204263	8.81	10.21
Immunoglobulin superfamily, member 1	XM_003643874	6.02	3.85
Inverted formin, FH2 and WH2 domain	XM_421396	4.86	3.46
Interferon regulatory factor 5	NM_001031587	6.69	6.98
Janus kinase 3	NM_204996	7.68	7.97
Lysosomal protein transmembrane 5	XM_417701	8.86	9.12
Macrophage receptor with collagenous structure	NM_204736	8.43	8.27
Muscleblind-like	NM_001163327	8.02	7.94
Microtubule associated monooxygenase, calponin and LIM	NM_001031576	8.06	8.63

Gene name	Accession no	Fold changes	
		Line 6.3	Line 7.2
Myosin IF	NM_205254	7.01	7.30
NUAK family, SNF1-like kinase	XM_416310	5.76	5.43
OTU domain containing 1	XM_418604	7.58	6.41
Purinergic receptor P2Y	NM_001008679	7.21	7.17
Phosphatidylinositol transfer protein, beta	NM_001039266	6.63	6.65
Pleckstrin	NM_204863	7.78	7.33
Protein phosphatase 1, regulatory (inhibitor) subunit 9B	XM_003644026.1	7.72	7.97
Protein tyrosine phosphatase, receptor type, C	NM_204417	8.57	8.71
Quaking homolog, KH domain RNA binding	NM_204310	7.07	6.79
Ras association (RalGDS/AF-6) domain family member 2	NM_001030884	7.29	7.33
Ribosomal protein L29	NM_001171677	10.74	11.22
Leukocyte ribonuclease A-2	NM_001007942	8.33	8.47
Selectin E	XM_422207.3	7.22	6.86
Small ArfGAP2	NM_001030902	7.93	7.96
SPEG complex locus	XM_004176748	0	7.20
Spi-C transcription factor	XM_425488	6.69	6.46
Serine/threonine kinase 38	XM_003642721	6.62	6.57
Synaptonemal complex central element protein 3	XM_001231763	0	7.61
Transcription factor 7 (T-cell specific, HMG-box)	NM_204547	6.68	7.08
Transforming growth factor, beta-induced	NM_205036	6.84	6.63
Tetratricopeptide repeat domain 27	NM_001012567	4.79	4.97
Unc-119 homolog B	XM_415263	6.36	6.23
WDFY family member 4	XM_003641478	6.25	6.39
Zinc finger E-box binding homeobox 2	XM_422151	6.30	5.93
Allograft inflammatory factor 1-like	XM_415461	8.34	8.20
Argininosuccinate synthase 1 (ASS1)	NM_001013395	7.97	8.24
ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, beta 3 polypeptide	NM_205535	5.85	5.81
Avidin-related protein 4/5-like	XM_001233209	4.97	8.95
Uncharacterized LOC419592	XM_417739	8.59	8.44
Carbonic anhydrase 13-like	XM_003640811	6.94	5.15
Chemokine (C-C Motif) Ligand	XM_415780	6.39	7.30
C-type lectin domain family 17	XM_423779	6.01	6.41
Complement receptor type 2-like	XM_001235095	5.79	5.85
Friend leukemia virus integration 1 (FLI1)	M_001030908	6.94	6.72
DEAD (Asp-Glu-Ala-Asp) box polypeptide 17	XM_416260	8.56	8.65
Major histocompatibility complex class II beta chain	S66480	10.15	10.49
Viral interleukin-8 homolog	XM_420473	8.09	7.96
Chicken Ig rearranged light-chain mRNA V-J-C region	CHKIGLAVD	10.72	12.12
ADP-ribosylation factor-like 4C (ARL4C)	XM_001237034	6.02	5.66
Actin related protein 2/3 complex, subunit 5, 16kDa ARPC5)	NM_001031561	10.12	10.58
Bruton agamma globulinemia tyrosine kinase (BTK)	NM_204233	6.60	6.64
Coiled-coil domain containing 165	XM_423729	0	7.13
Clusterin (CLU)	NM_204900	9.30	9.40
Colony stimulating factor 1 receptor(CSF1R)	XM_414597	7.46	6.93
Tyrosine kinase protooncogene (c-tkl)	CHKTCKL	6.86	6.90
Ganglioside GM2 activator-like	XM_003642059	7.68	6.43
Hemoglobin, gamma A (HBG1)	NM_001004390	11.31	8.71
Histone deacetylase 8 (HDAC8)	XM_420178	9.96	10.49
Hermansky-Pudlak syndrome 5 (HPS5)	XM_421011	8.74	8.13
Heat shock protein Hsp70 (hsp70) gene	AY143692	9.46	8.55
Immunoglobulin heavy chain variable region (IGVH gene)	AM773251	10.03	-0.32
Immunoglobulin heavy chain variable region (IGVH gene)	AM773267	9.56	5.96
GTPase IMAP family member 8-like	XM_418473	7.12	6.73



Gene name	Accession no	Fold changes	
		Line 6.3	Line 7.2
Integrin, alpha 4 (alpha 4 subunit of VLA-4 receptor)	XM_421974	7.55	7.44
Integrin, beta 2 (complement component 3 receptor 3 and 4)	NM_205251	8.27	8.54
Integrin beta 3 (platelet glycoprotein IIIa, antigen CD61)	NM_204315	6.57	4.72
Janus kinase 1 (JAK1)	NM_204870	8.35	8.30
Lymphocyte cytosolic protein 1 (L-plastin)	NM_001008440	9.01	8.88
Leukocyte cell-derived chemotaxin 2	NM_205478	7.67	2.04
Lymphocyte-specific protein 1	NM_204342	8.57	8.61
126 MRP mRNA	X61200	9.37	9.52
Moesin (MSN)	XR_140102	8.87	8.83
Nerve growth factor receptor	NM_001146133	6.46	6.62
Nucleophosmin (nucleolar phosphoprotein B23, numatrin)	NM_205267	11.14	11.41
Protein kinase C, beta	XM_414868	7.43	7.59
Ribosomal protein S6	NM_205225	9.81	10.54
Septin 6 (SEPT6)	NM_001031125	7.98	8.09
GB-2 T cell receptor alpha	GDU04611	7.57	7.95
AA2 T cell receptor beta	EF554758	7.91	8.54
Transmembrane protein 123 (TMEM123)	NM_001006279	7.82	8.17
Ig germline heavy chain VD region (VH15-9)	CHKIGVHAH	9.37	7.58
Ig germline heavy chain VD region (VH57-1)pseudogene.	CHKIGVHAJ	9.19	7.26
Ig germline heavy chain VD region (VH57-13)	CHKIGVHAR	7.38	7.53
Zinc finger protein 598, transcript variant 3 (ZNF598)	XM_414850	6.96	7.15
Gatinaise disrupted tyrosinase gene, intron 4	DQ118701	11.06	-1.74
Hemoglobin subunit alpha-A-like	XM_003643191	11.84	8.53
High mobility group 1 protein	Y17968	8.76	8.42
Hypothetical protein, clone 8j21	AJ719941	10.66	10.81
Ig heavy-chain gene V region	CHKIGHC	8.72	7.80
Ig rearranged H-chain gene V-D-J-region	CHKIGHAZE	10.52	7.71
Ig rearranged H-chain gene V-D-J-region	CHKIGHAZE	12.45	11.15
Ig rearranged heavy chain V region (VH1)	CHKIGVHAAK	8.49	7.94
Ig rearranged lambda-chain pseudogene psi-V14 V1 region	CHKIGLA12	8.25	6.48
Ig rearranged lambda-chain pseudogene psi-V7 V1 region	CHKIGLA19	9.45	7.02
Immunoglobulin alpha heavy chain	S40610	7.74	5.00
Mitochondrial genome	X52392	12.53	12.30
Ras-related protein Rab-10-like	XM_419183	5.79	5.46
SH2 domain-containing adapter protein E-like	XM_003643441	10.53	7.62
T-cell-interacting, activating receptor on myeloid cells protein 1-like	XM_003644001	6.60	0
T-lymphocyte surface antigen Ly-9-like	XM_003642660	6.86	7.24
Transmembrane 6 superfamily member 2-like	XM_423447	0	8.26
Uncharacterized LOC415472	XM_429332	5.85	6.42

**Supplementary Table S4.** Description of cytokine and receptor genes in the spleens of chicken lines 6.3 and 7.2 responsive to co-infection with EM/CP. The data showed significant changes in gene expression of the 53 cytokine genes and 97 cytokine receptor genes in NE-afflicted chicken lines. The genes included here showed significant differences in gene expression ( $p < 0.01$ , Log2-transformations of the normalization).

Gene	Full name	Fold changes	
		Line 6.3	Line 7.2
ADIPOQ	Adiponectin, C1Q And Collagen	8.15	8.41
BMP2K	BMP-2-Inducible Protein Kinase	2.04	1.75
BMPER	BMP Binding Endothelial Regulator	-3.10	-3.82
CCL1	Chemokine (C-C Motif) Ligand 1	-1.25	1.57
CCL17	Chemokine (C-C Motif) Ligand 17	-0.20	-0.19
CCL19	Chemokine (C-C Motif) Ligand 19	-2.30	2.70
CCL20	Chemokine (C-C Motif) Ligand 20	-3.77	-3.62
CCL3	Chemokine (C-C Motif) Ligand 3	3.42	4.68
CCL4	Chemokine (C-C Motif) Ligand 1	1.85	5.78
CMC1	COX Assembly Mitochondrial Protein 1 Homolog	-0.60	0.32
CNTF	Ciliary Neurotrophic Factor	0.93	3.45
CXCL13	Chemokine (C-X-C Motif) Ligand 13	9.25	2.93
CXCL14	Chemokine (C-X-C Motif) Ligand 14	-2.66	-3.95
FASLG	Fas Ligand (TNF Superfamily, Member 6)	-1.74	1.95
IFITM10	Interferon Induced Transmembrane Protein 10	0.00	0.00
IFNA1	Interferon, Alpha 1	1.92	-0.59
IFNB	Interferon, Beta	-2.64	2.62
IFNG	Interferon, Gamma	-1.80	1.48
IFNK	Interferon, Kappa	-1.57	-1.81
IL-10	Interleukin 10	0.50	2.32
IL-12A	Interleukin 12A	-2.81	0.99
IL-16	Interleukin 16	2.06	2.05
IL-17B	Interleukin 17B	-2.57	0.00
IL-17D	Interleukin 17D	-3.94	-3.62
IL-17F	Interleukin 17F	-3.40	-0.61
IL-19	Interleukin 19	-2.87	0.48
IL-22	Interleukin 22	-7.48	-5.77
IL-26	Interleukin 26	-7.08	-4.93
IL-28B	Interleukin 28B	2.98	-0.30
IL-34	Interleukin 34	2.94	2.94
IL-5	Interleukin 5	0.44	-0.04
IL-6	Interleukin 6	0.95	1.60
IL-7	Interleukin 7	-2.73	2.03
IL-8	Interleukin 8	-0.77	-0.12
ILF2	Interleukin Enhancer Binding Factor 2	0.66	0.76
LIF	Leukemia Inhibitory Factor	-2.38	0.76
NLRC3	NLR Family, CARD Domain Containing 3	-2.64	-0.46
NLRC5	NLR Family, CARD Domain Containing 5	-1.16	-0.63
NRG4	Neuregulin 4	-1.48	-1.89
SPP1	Secreted Phosphoprotein 1	2.50	0.35
SPP2	Secreted Phosphoprotein 2	-0.08	2.43
TAP1	Transporter 1, ATP-Binding Cassette, Sub-Family B	0.11	1.10
TAP2	Transporter 2, ATP-Binding Cassette, Sub-Family B	0.26	0.55
TGFA	Transforming Growth Factor, Alpha	-2.05	-0.80

Gene	Full name	Fold changes	
		Line 6.3	Line 7.2
TGFB1	Transforming Growth Factor, Beta 1	7.34	7.46
TNFAIP2	Tumor Necrosis Factor, Alpha-Induced Protein 2	4.97	4.64
TNFAIP3	Tumor Necrosis Factor, Alpha-Induced Protein 3	2.11	2.53
TNFAIP8	Tumor Necrosis Factor, Alpha-Induced Protein 8	2.45	2.42
TNFAIP8L1	Tumor Necrosis Factor, Alpha-Induced Protein 8 Like 1	2.80	2.94
TNFAIP8L3	Tumor Necrosis Factor, Alpha-Induced Protein 8 Like 3	0.04	3.96
TNFSF11	Tumor Necrosis Factor (Ligand) Superfamily, Member 11	3.52	1.64
TNFSF13B	Tumor Necrosis Factor (Ligand) Superfamily, Member 13B	6.70	4.69
VEGFA	Vascular Endothelial Growth Factor A	-4.24	-5.06
CSF2RA	Colony Stimulating Factor 2 Receptor, Alpha	5.23	7.77
CSF2RB	Colony Stimulating Factor 2 Receptor, Beta	5.33	7.68
CSF3R	Colony Stimulating Factor 3 Receptor	10.16	8.52
CXCR3	Chemokine (C-X-C Motif) Receptor 3	-8.22	-7.88
CXCR7	Chemokine (C-X-C Motif) Receptor 7	4.33	2.40
GDF8	Growth differentiation factor 8	0.00	1.87
IFIH1	Interferon Induced With Helicase C Domain 1	-1.46	-0.16
IFITM5	Interferon Induced Transmembrane Protein 5	-8.38	-4.84
IFNAR1	Interferon (Alpha, Beta And Omega) Receptor 1	0.98	2.09
IFNAR2	Interferon (Alpha, Beta And Omega) Receptor 2	0.78	1.03
IFNGR1	Interferon Gamma Receptor 1	1.75	0.95
IFNGR2	Interferon Gamma Receptor 2	-0.64	0.08
IGF1R	Insulin-Like Growth Factor 1 Receptor	1.53	1.43
IL-11RA	Interleukin 11 Receptor, Alpha	0.92	-3.29
IL-12RB1	Interleukin 12 Receptor, Beta 1	1.91	0.84
IL-12RB2	Interleukin 12 Receptor, Beta 2	0.89	1.32
IL-13RA1	Interleukin 13 Receptor, Alpha 1	-2.86	-1.92
IL-17RA	Interleukin 17 Receptor, Alpha	2.39	2.08
IL-17RC	Interleukin 17 Receptor C	-4.96	-5.02
IL-17RD	Interleukin 17 Receptor D	-1.25	-2.70
IL-17REL	Interleukin 17 Receptor E-Like	1.58	4.28
IL-18R1	Interleukin 18 Receptor 1	5.88	5.01
IL-18RAP	Interleukin 18 Receptor Accessory Protein	6.13	3.11
IL-1R1	Interleukin 1 Receptor 1	6.49	1.97
IL-1R2	Interleukin 1 Receptor 2	3.55	7.91
IL-1RAP	Interleukin 1 Receptor Accessory Protein	6.63	5.81
IL-1RAPL2	Interleukin 1 Receptor Accessory Protein-Like 2	-5.00	-4.99
IL-1RL1	Interleukin 1 Receptor-Like 1	2.82	6.98
IL-1RL2	Interleukin 1 Receptor-Like 2	4.46	-0.07
IL-20RA	Interleukin 20 Receptor, Alpha	2.48	3.59
IL-20RB	Interleukin 20 Receptor, Beta	1.53	2.23
IL-21R	Interleukin 21 Receptor	3.04	3.49
IL-22RA1	Interleukin 22 Receptor, Alpha 1	-10.08	-9.12
IL-22RA2	Interleukin 22 Receptor, Alpha 2	-2.11	-2.43
IL-23R	Interleukin 23 Receptor	1.71	-0.34
IL-28RA	Interleukin 28 Receptor, Alpha	-1.43	-1.03
IL-2RB	Interleukin 2 Receptor, Beta	2.20	1.54
IL-2RG	Interleukin 2 Receptor, Gamma	3.56	3.58
IL-31RA	Interleukin 31 Receptor, Alpha	6.40	4.78
IL-4I1	Interleukin 4 Induced 1	2.23	3.92
IL-4R	Interleukin 4 Receptor	1.71	1.64

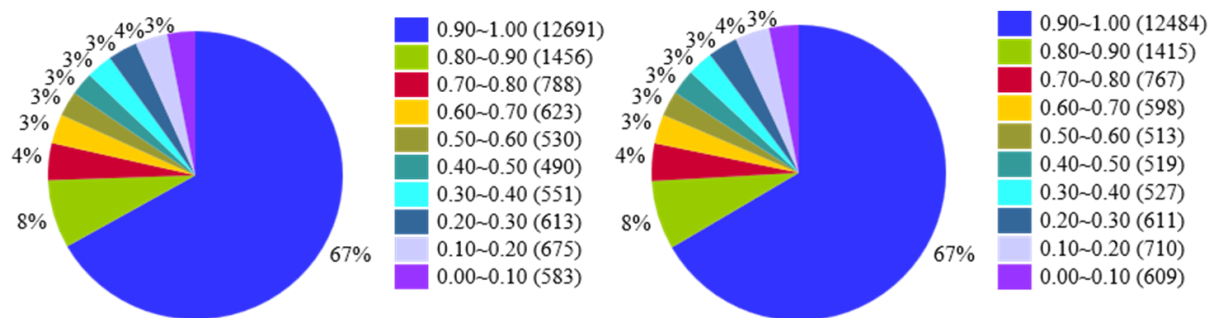
Gene	Full name	Fold changes	
		Line 6.3	Line 7.2
IL-5RA	Interleukin 5 Receptor, Alpha	7.26	1.22
IL-6ST	Interleukin 6 Signal Transducer	6.02	5.67
IL-7R	Interleukin 7 Receptor	10.67	8.23
IL-9R	Interleukin 9 Receptor	5.31	4.90
ILDR1	Immunoglobulin-Like Domain Containing Receptor 1	-3.04	-2.78
ILDR2	Immunoglobulin-Like Domain Containing Receptor 2	1.54	2.60
ILF3	Interleukin Enhancer Binding Factor 3	1.02	1.22
LEPRE1	Leucine Proline-Enriched Proteoglycan (Leprecan) 1	1.31	1.73
LEPREL1	Leprecan-Like 1	3.61	-2.15
LEPREL2	Leprecan-Like 2	-0.86	-3.41
LEPREL4	Leprecan-Like 4	-0.24	0.52
LEPROTL1	Leptin Receptor Overlapping Transcript-Like 1	0.51	1.34
LIFR	Leukemia Inhibitory Factor Receptor Alpha	2.72	3.66
LILRA2	Leukocyte Immunoglobulin-Like Receptor, Subfamily A, Member 2	5.09	1.75
LILRA4	Leukocyte Immunoglobulin-Like Receptor, Subfamily A, Member 4	0.82	-0.54
LILRA5	Leukocyte Immunoglobulin-Like Receptor, Subfamily A, Member 5	-2.17	-2.14
LILRA6	Leukocyte Immunoglobulin-Like Receptor, Subfamily A, Member 6	4.99	0.00
LILRB1	Leukocyte Immunoglobulin-Like Receptor, Subfamily B, Member 1	2.47	4.64
LILRB3	Leukocyte Immunoglobulin-Like Receptor, Subfamily B, Member 3	5.49	0.58
LILRB4	Leukocyte Immunoglobulin-Like Receptor, Subfamily B, Member 4	3.24	2.52
LILRB5	Leukocyte Immunoglobulin-Like Receptor, Subfamily B, Member 5	4.31	3.65
LTB4R	Leukotriene B4 Receptor	7.16	7.33
LTBP1	Latent Transforming Growth Factor Beta Binding Protein 1	1.65	1.75
LTBP2	Latent Transforming Growth Factor Beta Binding Protein 2	-3.63	-3.18
MC1R	Melanocortin 1 Receptor	0.00	-2.65
NRG2	Neuregulin 2	-0.09	-4.76
NRG3	Neuregulin 3	0.38	0.00
PDGFC	Platelet Derived Growth Factor C	1.79	-1.03
PDGFD	Platelet Derived Growth Factor D	-2.19	2.30
PDGFRL	Platelet-Derived Growth Factor Receptor, Alpha Polypeptide	-4.61	-0.03
TGFBR2	Transforming Growth Factor, Beta Receptor II	2.18	0.96
TGFBRAP1	Transforming Growth Factor, Beta Receptor Associated Protein 1	1.22	0.40
TGFBR1	Transforming Growth Factor, Beta Receptor I	3.91	3.41
TLR1	Toll-Like Receptor 1	3.34	4.11
TLR15	Toll-Like Receptor 15	5.30	8.26
TLR21	Toll-Like Receptor 21	4.32	2.23
TLR5	Toll-Like Receptor 5	2.28	-0.47
TLR6	Toll-Like Receptor 6	3.82	5.46
TLR7	Toll-Like Receptor 7	8.04	7.08
TNFRSF11A	Tumor Necrosis Factor Receptor Superfamily, Member 11a,	-0.88	-1.59
TNFRSF11B	Tumor Necrosis Factor Receptor Superfamily, Member 11b	-0.19	-1.00
TNFRSF13B	Tumor Necrosis Factor Receptor Superfamily, Member 13B	4.04	5.59
TNFRSF13C	Tumor Necrosis Factor Receptor Superfamily, Member 13C	6.73	7.94
TNFRSF14	Tumor Necrosis Factor Receptor Superfamily, Member 14	-4.47	-3.48
TNFRSF18	Tumor Necrosis Factor Receptor Superfamily, Member 18	1.28	1.84
TNFRSF1B	Tumor Necrosis Factor Receptor Superfamily, Member 1B	4.61	5.83
TNFRSF21	Tumor Necrosis Factor Receptor Superfamily, Member 21	0.90	1.75
TNFRSF25	Tumor Necrosis Factor Receptor Superfamily, Member 25	2.80	1.92
TNFRSF4	Tumor Necrosis Factor Receptor Superfamily, Member 4	-1.20	-1.20
TNFRSF6B	Tumor Necrosis Factor Receptor Superfamily, Member 6B	-6.36	-0.46

Gene	Full name	Fold changes	
		Line 6.3	Line 7.2
TNFRSF9	Tumor Necrosis Factor Receptor Superfamily, Member 9	1.63	1.98
TRAT1	T Cell Receptor Associated Transmembrane Adaptor 1	4.37	5.10
TRDC	T Cell Receptor Delta Constant	2.43	2.14
TRGC1	T Cell Receptor Gamma Constant 1	1.69	1.84
XCR1	Chemokine (C Motif) Receptor 1	6.65	6.25

**Supplementary Table S5.** Description of CD molecular genes responsive to NE- affliction in the spleen of the two chicken lines. The data showed significant changes in the gene expression of 44 CD molecular genes in the two NE-afflicted chicken lines. The genes included here showed significant differences in gene expression ( $p < 0.01$ , Log<sub>2</sub>-transformations of the normalization).

Symbols	Full gene name	Fold changes	
		Line 6.3	Line 7.2
CD2	CD2 Molecule	6.03	5.02
CD200	CD200 Molecule	5.62	6.03
CD200R1	CD200 Molecule receptor 1	1.14	-1.06
CD200R1A	CD200 Molecule receptor 1 Like	4.38	3.75
CD226	CD226 Molecule	1.42	0.65
CD244	CD244 Molecule	2.12	1.51
CD247	CD247 Molecule	2.71	3.27
CD274	CD274 Molecule	-0.13	2.54
CD276	CD276 Molecule	-0.09	0.73
CD28	CD28 Molecule	4.34	3.31
CD2AP	CD2 Molecule Associated Protein	-1.51	-1.50
CD300A	CD300A Molecule	1.38	1.69
CD300C	CD300C Molecule	1.86	1.05
CD300LF	CD300 molecule-like family member f	0.00	0.00
CD34	CD34 Molecule	-2.94	-1.18
CD36	CD36 Molecule	4.28	-5.01
CD38	CD38 Molecule	2.89	3.32
CD3D	T-Cell Surface Glycoprotein CD3 Delta	1.32	1.61
CD3E	T-Cell Surface Glycoprotein CD3 Epsilon	2.10	2.08
CD4	CD4 Molecule	5.86	6.15
CD40	CD40 Molecule	4.43	3.23
CD40L	CD40 Molecule Ligand	2.88	2.57
CD44	CD44 Molecule	3.49	3.69
CD5	CD5 Molecule	3.74	4.56
CD55	CD55 Molecule	-1.03	-1.15
CD59	CD59 Molecule	4.78	2.70
CD5L	CD5 Molecule-Like	3.25	3.31
CD69	CD69 Molecule	2.30	2.15
CD7	CD7 Molecule	-2.18	-0.62
CD72	CD72 Molecule	6.10	8.48
CD79B	CD79b molecule, immunoglobulin-associated beta	6.62	8.14
CD80	CD80 Molecule	1.37	1.70
CD8A	CD8a Molecule	-4.90	-1.56
CD93	CD93 Molecule	8.42	3.25
CD99	CD99 Molecule	-0.39	-0.46
CD99L2	CD99 molecule-like 2	0.99	-1.03
CD101	CD101 Molecule	-0.70	-1.60
CD109	CD109 Molecule	1.48	-0.62
CD14	CD14 Molecule	4.30	3.89

<b>Symbols</b>	<b>Full gene name</b>	<b>Fold changes</b>	
		<b>Line 6.3</b>	<b>Line 7.2</b>
CD163	CD163 Molecule	-8.26	-6.88
CD163L1	CD163 Molecule Like 1	4.20	1.28
CD180	CD180 Molecule	6.53	8.70
CD48	CD48 Molecule	-0.81	2.34
CD83	CD83 Molecule	3.95	4.69

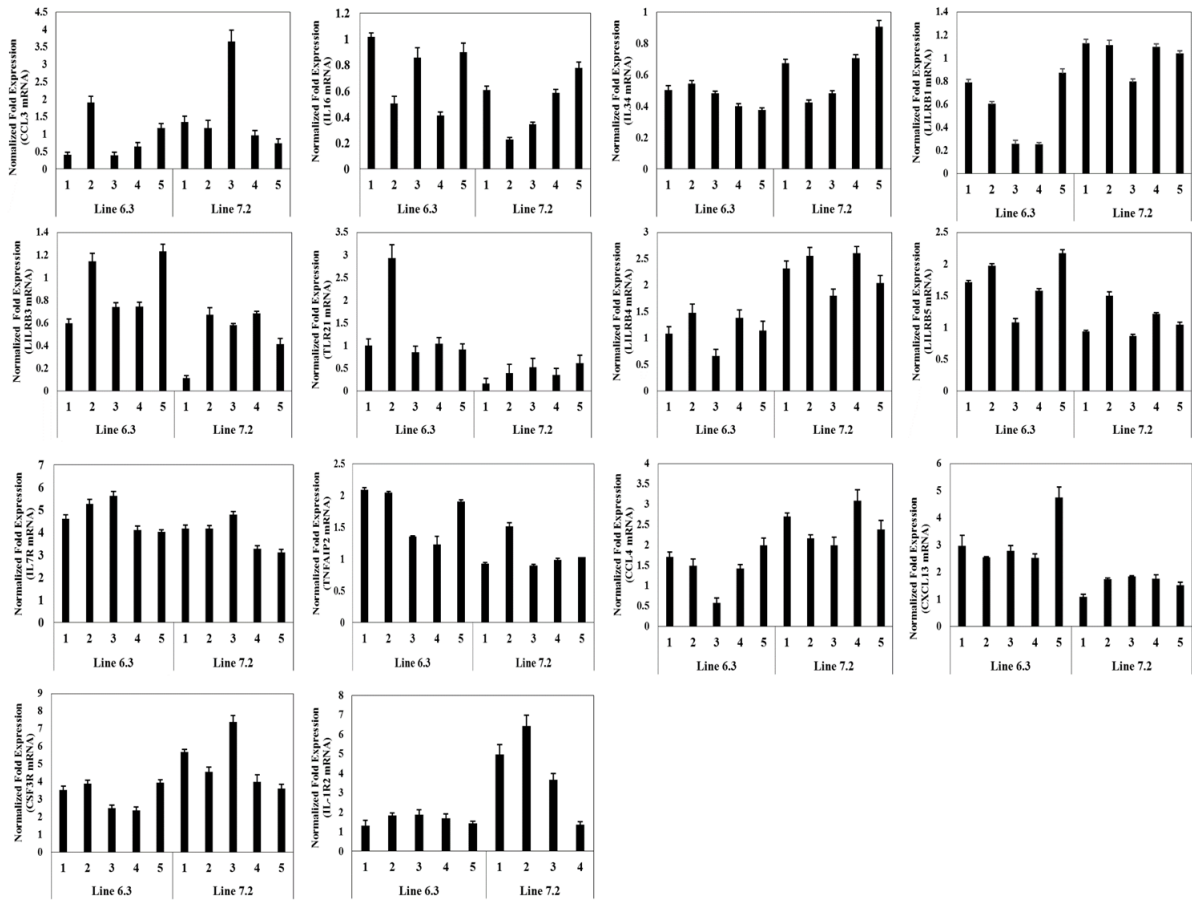


Distribution of Genes' Coverage in NE samples of line 6.3

Distribution of Genes' Coverage in NE samples of line 7.2

**Supplementary Figure S1.** Percent of coverage representing the percentage of genes expressed in the spleen of the two chicken lines. The distribution of distinct reads over different read abundance categories showed similar patterns for both RNA-Seq libraries. The similarity distribution displayed a comparable pattern with approximately 73% of the sequences having a similarity of 80%, while approximately 27% of the hits had a similar range in the spleen of lines 6.3 and 7.2.





**Supplementary Figure S2.** Normalized fold expression of cytokine genes in the spleen of individuals of the two genetically disparate lines (Line 6.3 and Line 7.2, control=1). Chickens were orally infected with  $1.0 \times 10^4$  oocysts of *E.maxima* on day 14 followed by infection with *C.perfringens* at  $1.0 \times 10^9$  CFU 4 days later. Spleens were isolated from 2-day post *C.P.* infected chickens, and transcriptional levels were determined by quantitative RT-PCR.