



Figure S1. Quantile-Quantile (QQ) plot of the expected vs. the observed null distribution of the P-values for the association between the 624,460 SNPs and 1,967 dairy cattle across three herds diagnosed with at least one disease in the metritis complex.

Table S1. Identified single nucleotide polymorphisms (SNPs) with flanking candidate genes and associated quantitative trait loci (QTL).

BTA ¹	SNP-ID ²	P-value ³	SNP Position**	Candidate gene ⁴	Linked Trait ⁵	QTL ID
12	BovineHD1200009956	3.30E-06	33569134	ATP8A2	Non-return rate	QTL:5010
10	BovineHD1000023339	2.36E-05	81497245	SRSF5	Dystocia	QTL:11353
10	BovineHD1000023340	2.36E-05	81497728	SRSF5	Dystocia	QTL:11353
10	BTB-02098111	3.03E-05	81532849	SLC10A1	Dystocia	QTL:11444
10	BovineHD1000023344	3.05E-05	81512830	SLC10A1	Dystocia	QTL:11444
10	BovineHD1000023769	3.31E-05	83080675	SIPA1L1	Stillbirth	QTL:11445
10	BTA-77307-no-rs	3.96E-05	81502058	SRSF5	Dystocia	QTL:11353
17	BovineHD1700021176	4.33E-05	70481417	DEPDC5	Non-return rate	QTL:141715
10	BovineHD1000023497	5.78E-05	82066559	COX16	Stillbirth	QTL:11445
15	BovineHD1500002327	7.55E-05	8809053	CNTN5	Non-return rate	QTL:3571
11	BovineHD0500026389	8.59E-05	92476148	DAB2IP	Stillbirth	QTL:126867
10	BovineHD1000025233	9.64E-05	87632404	ESRRB	Placental Retention	QTL:11316
21	BovineHD2100020220	1.03E-04	67602910	TRAF3 AMN	____ ____	____ ____
8	BovineHD0800007389	1.05E-04	24598682	SLC24A2	Stillbirth	QTL:11443
10	BovineHD1000025221	1.13E-04	87619311	ESRRB	Placental Retention	QTL:11316
10	BovineHD1000023418	1.15E-04	81811346	SLC8A3	Dystocia	QTL:11353
10	BovineHD1000025236	1.27E-04	87637414	ESRRB	Placental Retention	QTL:11316
10	BovineHD1000025235	1.27E-04	87634538	ESRRB	Placental Retention	QTL:11316
11	BovineHD1100026876	1.28E-04	92476478	DAB2IP	Stillbirth	QTL:126867

¹ BTA =Bos taurus autosome

² SNP = Single nucleotide polymorphism; SNPs listed in ascending order with respect to P-value

³ Genome-wide significance threshold

⁴ Nearest gene 10k base pair downstream/upstream relative to the SNP

⁵ Previously associated trait; Details obtained from the Animal QTLdb for cattle [36]

27	BovineHD2700007980	1.31E-04	29252315	<i>RNF122</i>	Dystocia	QTL:11393
17	BovineHD1700019549	1.33E-04	65237605	<i>KIAA1671</i>	Calving ease	QTL:11051
11	BovineHD1100026874	1.33E-04	92473780	<i>DAB2IP</i>	Stillbirth	QTL:126867
11	BovineHD1100026881	1.37E-04	92481234	<i>DAB2IP</i>	Stillbirth	QTL:126867
10	BovineHD1000025230	1.39E-04	87629150	<i>ESRRB</i>	Placental Retention	QTL:11316
11	BovineHD1100026880	1.59E-04	92480213	<i>DAB2IP</i>	Stillbirth	QTL:126867
4	BovineHD0400018341	1.71E-04	66416290	<i>SCRN1</i>	Calving Ease	QTL:10713
				<i>WIPF3</i>	Calving Ease	QTL:10713
10	BovineHD1000025232	1.73E-04	87631188	<i>ESRRB</i>	Placental Retention	QTL:11316
10	BovineHD1000025229	1.73E-04	87628421	<i>ESRRB</i>	Placental Retention	QTL:11316
10	BovineHD1000025231	1.75E-04	87630598	<i>ESRRB</i>	Placental Retention	QTL:11316
8	BovineHD0800007387	1.76E-04	24596562	<i>SLC24A2</i>	Stillbirth	QTL:11443
11	BovineHD1100026875	1.86E-04	92475887	<i>DAB2IP</i>	Stillbirth	QTL:126867
11	BovineHD1100026877	1.95E-04	92477673	<i>DAB2IP</i>	Stillbirth	QTL:126867
10	BovineHD1000025228	2.09E-04	87627458	<i>ESRRB</i>	Placental Retention	QTL:11316
10	BovineHD1000023822	2.15E-04	83245103	<i>SIPA1L1</i>	Stillbirth	QTL:11445
25	BovineHD2500009545	2.20E-04	34170987	<i>POR</i>	Calving ease	QTL:4674
8	BovineHD0800007390	2.26E-04	24599571	<i>SLC24A2</i>	Stillbirth	QTL:11443
11	BovineHD1100005785	2.38E-04	18909925	<i>CRIM1</i>	-	-
10	BovineHD1000025245	2.44E-04	87650109	<i>ESRRB</i>	Placental Retention	QTL:11316
18	BovineHD1800003585	2.47E-04	10026821	<i>CDH13</i>	Dystocia	QTL:2707

Table S2. Enriched gene ontology (GO) biological process (BP) terms for the metritis complex in Jersey and Holstein dairy cattle.

GO-ID ⁶	Term	p-value	Gene(s) Assoc. ⁷
GO:0098703	Calcium Ion Import Across Plasma Membrane	0.015	<i>SLC8A3, SLC24A2</i>
GO:0032088	Negative Regulation of NF-KappaB Transcription Factor Activity	0.062	<i>DAB2IP, TRAF3</i>
GO:0043087	Regulation of GTPase Activity	0.065	<i>DAB2IP, SIPA1L1</i>
GO:0046330	Positive Regulation of JNK Cascade	0.076	<i>DAB2IP, TRAF3</i>
GO:0043065	Positive Regulation of Apoptotic Process	0.184	<i>DAB2IP, RNF122</i>
GO:0008285	Negative Regulation of Cell Proliferation	0.214	<i>CDH13, DAB2IP</i>
GO:0045944	Positive Regulation of Transcription from RNA Polymerase II Promoter	0.510	<i>CDH13, DAB2IP</i>
GO:1900744	Regulation of P38Mapk Cascade	1.000	<i>DAB2IP</i>
GO:0070317	Negative Regulation of G0 to G1 Transition	1.000	<i>DAB2IP</i>
GO:0030032	Lamellipodium Assembly	1.000	<i>CDH13</i>
GO:0048661	Positive Regulation of Smooth Muscle Cell Proliferation	1.000	<i>CDH13</i>
GO:0050680	Negative Regulation of Epithelial Cell Proliferation	1.000	<i>DAB2IP</i>
GO:0043124	Negative Regulation of I-KappaB Kinase/NF-KappaB Signaling	1.000	<i>DAB2IP</i>
GO:0007162	Negative Regulation of Cell Adhesion	1.000	<i>CDH13</i>
GO:0043542	Endothelial Cell Migration	1.000	<i>CDH13</i>
GO:0014067	Negative Regulation of Phosphatidylinositol 3-Kinase Signaling	1.000	<i>DAB2IP</i>
GO:0070588	Calcium Ion Transmembrane Transport	1.000	<i>SLC24A2</i>

⁶ GO-ID = Gene Ontology Identification Number

⁷ Gene(s) Assoc. = Genes linked to significant genetic variants in the metritis complex GWAS *in-silico* functional analysis

GO:0030335	Positive Regulation of Cell Migration	1.000	CDH13
GO:0010917	Negative Regulation of Mitochondrial Membrane Potential	1.000	RNF122
GO:0007156	Homophilic Cell Adhesion Via Plasma Membrane Adhesion Molecules	1.000	CDH13
GO:0051865	Protein Autoubiquitination	1.000	RNF122
GO:0090346	Cellular Organofluorine Metabolic Process	1.000	POR
GO:0036324	Vascular Endothelial Growth Factor Receptor-2 Signaling Pathway	1.000	DAB2IP
GO:0050688	Regulation of Defense Response to Virus	1.000	TRAF3
GO:0070534	Protein K63-Linked Ubiquitination	1.000	TRAF3
GO:0034260	Negative Regulation of GTPase Activity	1.000	DAB2IP
GO:0007588	Excretion	1.000	AMN
GO:0034198	Cellular Response to Amino Acid Starvation	1.000	DEPDC5
GO:0007613	Memory	1.000	SLC24A2
GO:0043161	Proteasome-Mediated Ubiquitin-Dependent Protein Catabolic Process	1.000	RNF122
GO:0048814	Regulation of Dendrite Morphogenesis	1.000	SIPA1L1
GO:0015914	Phospholipid Transport	1.000	ATP8A2
GO:0050927	Positive Regulation of Positive Chemotaxis	1.000	CDH13
GO:0000122	Negative Regulation of Transcription from RNA Polymerase II Promoter	1.000	DAB2IP
GO:0050770	Regulation of Axonogenesis	1.000	SIPA1L1
GO:0060292	Long Term Synaptic Depression	1.000	SLC24A2
GO:0043122	Regulation of I-KappaB Kinase/NF-KappaB Signaling	1.000	TRAF3
GO:0045332	Phospholipid Translocation	1.000	ATP8A2
GO:0007601	Visual Perception	1.000	SLC24A2
GO:0021814	Cell Motility Involved in Cerebral Cortex Radial Glia Guided Migration	1.000	DAB2IP

GO:0008625	Extrinsic Apoptotic Signaling Pathway Via Death Domain Receptors	1.000	DAB2IP
GO:1900006	Positive Regulation of Dendrite Development	1.000	DAB2IP
GO:0035556	Intracellular Signal Transduction	1.000	DEPDC5
GO:0030514	Negative Regulation of Bmp Signaling Pathway	1.000	CRIM1
GO:0030048	Actin Filament-Based Movement	1.000	WIPF3
GO:0090630	Activation of GTPase Activity	1.000	SIPA1L1
GO:0035148	Tube Formation	1.000	DAB2IP
GO:0030948	Negative Regulation of Vascular Endothelial Growth Factor Receptor Signaling Pathway	1.000	DAB2IP
GO:0030001	Metal Ion Transport	1.000	SLC8A3
GO:0051056	Regulation of Small GTPase Mediated Signal Transduction	1.000	SIPA1L1
GO:0006357	Regulation of Transcription from RNA Polymerase II Promoter	1.000	ESRRB
GO:0098742	Cell-Cell Adhesion Via Plasma-Membrane Adhesion Molecules	1.000	CDH13
GO:0010506	Regulation of Autophagy	1.000	DEPDC5
GO:0016339	Calcium-Dependent Cell-Cell Adhesion Via Plasma Membrane Cell Adhesion Molecules	1.000	CDH13
GO:0045668	Negative Regulation of Osteoblast Differentiation	1.000	CRIM1
GO:0048147	Negative Regulation of Fibroblast Proliferation	1.000	DAB2IP
GO:0043616	Keratinocyte Proliferation	1.000	CDH13
GO:0010596	Negative Regulation of Endothelial Cell Migration	1.000	DAB2IP
GO:0000398	MRNA Splicing, Via Spliceosome	1.000	SRSF5
GO:0043407	Negative Regulation of Map Kinase Activity	1.000	DAB2IP
GO:0070373	Negative Regulation of Erk1 and Erk2 Cascade	1.000	DAB2IP
GO:2001224	Positive Regulation of Neuron Migration	1.000	DAB2IP
GO:0007154	Cell Communication	1.000	SLC8A3

GO:0048013	Ephrin Receptor Signaling Pathway	1.000	<i>SIPA1L1</i>
GO:0030162	Regulation of Proteolysis	1.000	<i>TRAF3</i>
GO:0044257	Cellular Protein Catabolic Process	1.000	<i>DAB2IP</i>
GO:0090129	Positive Regulation of Synapse Maturation	1.000	<i>DAB2IP</i>
GO:0021819	Layer Formation in Cerebral Cortex	1.000	<i>DAB2IP</i>
GO:0001817	Regulation of Cytokine Production	1.000	<i>TRAF3</i>
GO:0060291	Long-Term Synaptic Potentiation	1.000	<i>SLC24A2</i>
GO:0048666	Neuron Development	1.000	<i>ATP8A2</i>
GO:0030100	Regulation of Endocytosis	1.000	<i>CDH13</i>
GO:0031532	Actin Cytoskeleton Reorganization	1.000	<i>SIPA1L1</i>
GO:0038026	Reelin-Mediated Signaling Pathway	1.000	<i>DAB2IP</i>
GO:0007266	Rho Protein Signal Transduction	1.000	<i>CDH13</i>
GO:0031334	Positive Regulation of Protein Complex Assembly	1.000	<i>DAB2IP</i>
GO:0008063	Toll Signaling Pathway	1.000	<i>TRAF3</i>
GO:0032770	Positive Regulation of Monooxygenase Activity	1.000	<i>POR</i>
GO:0007252	I-KappaB Phosphorylation	1.000	<i>DAB2IP</i>
GO:1901800	Positive Regulation of Proteasomal Protein Catabolic Process	1.000	<i>DAB2IP</i>
GO:0043553	Negative Regulation of Phosphatidylinositol 3-Kinase Activity	1.000	<i>DAB2IP</i>
GO:0045087	Innate Immune Response	1.000	<i>TRAF3</i>
GO:0002224	Toll-Like Receptor Signaling Pathway	1.000	<i>TRAF3</i>
GO:0016525	Negative Regulation of Angiogenesis	1.000	<i>DAB2IP</i>
GO:0071222	Cellular Response to Lipopolysaccharide	1.000	<i>DAB2IP</i>
GO:0009725	Response to Hormone	1.000	<i>POR</i>
GO:0033617	Mitochondrial Respiratory Chain Complex Iv Assembly	1.000	<i>COX16</i>
GO:0006508	Proteolysis	1.000	<i>SCRN1</i>
GO:0034144	Negative Regulation of Toll-Like Receptor 4 Signaling Path-	1.000	<i>DAB2IP</i>

way			
GO:1903363	Negative Regulation of Cellular Protein Catabolic Process	1.000	DAB2IP
GO:0006874	Cellular Calcium Ion Homeostasis	1.000	SLC24A2
GO:0006887	Exocytosis	1.000	SCRN1
GO:0090090	Negative Regulation of Canonical WNT Signaling Pathway	1.000	DAB2IP
GO:0001954	Positive Regulation of Cell-Matrix Adhesion	1.000	CDH13
GO:0033209	Tumor Necrosis Factor-Mediated Signaling Pathway	1.000	TRAF3
GO:0032007	Negative Regulation of Tor Signaling	1.000	DEPDC5
GO:0015889	Cobalamin Transport	1.000	AMN
GO:0035924	Cellular Response to Vascular Endothelial Growth Factor Stimulus	1.000	DAB2IP
GO:0055096	Low-Density Lipoprotein Particle Mediated Signaling	1.000	CDH13
GO:0070059	Intrinsic Apoptotic Signaling Pathway in Response to Endo- plasmic Reticulum Stress	1.000	DAB2IP
GO:0015721	Bile Acid and Bile Salt Transport	1.000	SLC10A1
GO:0050850	Positive Regulation of Calcium-Mediated Signaling	1.000	CDH13
GO:0051668	Localization Within Membrane	1.000	CDH13
GO:0043507	Positive Regulation of Jun Kinase Activity	1.000	DAB2IP
GO:0001938	Positive Regulation of Endothelial Cell Proliferation	1.000	CDH13
GO:0006898	Receptor-Mediated Endocytosis	1.000	AMN
GO:0007612	Learning	1.000	SLC24A2
GO:0043001	Golgi to Plasma Membrane Protein Transport	1.000	AMN
GO:0022900	Electron Transport Chain	1.000	POR
GO:0008104	Protein Localization	1.000	AMN
GO:0071347	Cellular Response to Interleukin-1	1.000	DAB2IP
GO:2001235	Positive Regulation of Apoptotic Signaling Pathway	1.000	DAB2IP
GO:0032648	Regulation of Interferon-Beta Production	1.000	TRAF3

GO:0042981	Regulation of Apoptotic Process	1.000	<i>TRAF3</i>
GO:0015031	Protein Transport	1.000	<i>AMN</i>
GO:0035725	Sodium Ion Transmembrane Transport	1.000	<i>SLC8A3</i>
GO:0010719	Negative Regulation of Epithelial to Mesenchymal Transition	1.000	<i>DAB2IP</i>
GO:0002040	Sprouting Angiogenesis	1.000	<i>CDH13</i>
GO:0016601	RAC Protein Signal Transduction	1.000	<i>CDH13</i>
GO:0048812	Neuron Projection Morphogenesis	1.000	<i>DAB2IP</i>
GO:0042058	Regulation of Epidermal Growth Factor Receptor Signaling Pathway	1.000	<i>CDH13</i>
GO:0071356	Cellular Response to Tumor Necrosis Factor	1.000	<i>DAB2IP</i>
GO:1900747	Negative Regulation of Vascular Endothelial Growth Factor Signaling Pathway	1.000	<i>DAB2IP</i>

Table S3. Enriched gene ontology (GO) cellular component (CC) terms for the metritis complex in Jersey and Holstein dairy cattle.

GO-ID ⁸	Term	p-value	Gene(s) Assoc. ⁹
GO:0030139	Endocytic Vesicle	0.035	<i>DAB2IP, AMN</i>
GO:0005737	Cytoplasm	0.203	<i>CDH13, DEPDC5, RNF122, SIPA1L1, SCRNI, TRAF3</i>
GO:0016021	Integral Component of Membrane	0.343	<i>COX16, ATP8A2, POR, RNF122, CRIM1, SLC10A1, AMN, SLC8A3</i>
GO:0005887	Integral Component of Plasma Membrane	0.529	<i>SLC8A3, SLC24A2</i>
GO:0005886	Plasma Membrane	0.645	<i>ATP8A2, CDH13, SIPA1L1, AMN, SLC8A3</i>
GO:0005615	Extracellular Space	0.690	<i>CDH13, AMN</i>
GO:0005829	Cytosol	0.925	<i>SRSF5, POR</i>
GO:0005634	Nucleus	1.000	<i>ESRRB</i>
GO:0009897	External Side of Plasma Membrane	1.000	<i>CDH13</i>
GO:0043005	Neuron Projection	1.000	<i>CDH13</i>
GO:1990032	Parallel Fiber	1.000	<i>DAB2IP</i>
GO:0031965	Nuclear Membrane	1.000	<i>SCRNI</i>
GO:0005884	Actin Filament	1.000	<i>WIPF3</i>
GO:0005730	Nucleolus	1.000	<i>SRSF5</i>
GO:0005901	Caveola	1.000	<i>CDH13</i>
GO:0010008	Endosome Membrane	1.000	<i>ATP8A2</i>
GO:0042383	Sarcolemma	1.000	<i>SLC8A3</i>
GO:0098794	Post synapse	1.000	<i>SLC8A3</i>
GO:0097381	Photoreceptor Disc Membrane	1.000	<i>ATP8A2</i>
GO:0032809	Neuronal Cell Body Membrane	1.000	<i>DAB2IP</i>
GO:0012505	Endomembrane System	1.000	<i>RNF122</i>
GO:0035631	Cd40 Receptor Complex	1.000	<i>TRAF3</i>
GO:0015629	Actin Cytoskeleton	1.000	<i>SIPA1L1</i>
GO:0031305	Integral Component of Mitochondrial Inner Membrane	1.000	<i>COX16</i>

⁸GO-ID = Gene Ontology Identification Number

⁹Gene(s) Assoc. = Genes linked to significant genetic variants in the metritis complex GWAS in-silico functional analysis

GO:0031225	Anchored Component of Membrane	1.000	<i>CDH13</i>
GO:0005789	Endoplasmic Reticulum Membrane	1.000	<i>POR</i>
GO:0016342	Catenin Complex	1.000	<i>CDH13</i>
GO:0044301	Climbing Fiber	1.000	<i>DAB2IP</i>
GO:0043235	Receptor Complex	1.000	<i>AMN</i>
GO:0016020	Membrane	1.000	<i>SLC8A3</i>
GO:0005743	Mitochondrial Inner Membrane	1.000	<i>COX16</i>
GO:1990597	Aip1-Ire1 Complex	1.000	<i>DAB2IP</i>
GO:0030424	Axon	1.000	<i>SLC8A3</i>
GO:0005765	Lysosomal Membrane	1.000	<i>DEPDC5</i>
GO:0016324	Apical Plasma Membrane	1.000	<i>AMN</i>
GO:0009898	Cytoplasmic Side of Plasma Membrane	1.000	<i>TRAF3</i>
GO:0005794	Golgi Apparatus	1.000	<i>ATP8A2</i>
GO:0001917	Photoreceptor Inner Segment	1.000	<i>ATP8A2</i>
GO:1990531	Lem3P-Dnf1P Complex	1.000	<i>ATP8A2</i>
GO:0016607	Nuclear Speck	1.000	<i>SRSF5</i>
GO:1990130	Iml1 Complex	1.000	<i>DEPDC5</i>
GO:0044300	Cerebellar Mossy Fiber	1.000	<i>DAB2IP</i>
GO:0000139	Golgi Membrane	1.000	<i>ATP8A2</i>
GO:0005768	Endosome	1.000	<i>ATP8A2</i>
GO:0005576	Extracellular Region	1.000	<i>CRIM1</i>
GO:0005654	Nucleoplasm	1.000	<i>ATP8A2</i>
GO:0048471	Perinuclear Region of Cytoplasm	1.000	<i>SLC8A3</i>

Table S4. Enriched gene ontology (GO) molecular function (MF) terms for the metritis complex in Jersey and Holstein dairy cattle.

GO-ID ¹⁰	Term	P-value	Gene(s) Assoc. ¹¹
GO:0005096	GTPase Activator Activity	0.011	<i>DAB2IP, DEPDC5, SIPA1L1</i>
GO:0042803	Protein Homodimerization Activity	0.384	<i>CDH13, DAB2IP</i>
GO:0008270	Zinc Ion Binding	0.450	<i>ESRRB, TRAF3</i>
GO:0046872	Metal Ion Binding	0.749	<i>RNF122, SLC8A3</i>
GO:0031625	Ubiquitin Protein Ligase Binding	1.000	<i>TRAF3</i>
GO:0015491	Cation: Cation Antiporter Activity	1.000	<i>SLC8A3</i>
GO:0004879	RNA Polymerase II Transcription Factor Activity, Ligand-Activated Sequence-Specific DNA Binding	1.000	<i>ESRRB</i>
GO:0042802	Identical Protein Binding	1.000	<i>TRAF3</i>
GO:0005524	ATP Binding	1.000	<i>ATP8A2</i>
GO:0019901	Protein Kinase Binding	1.000	<i>TRAF3</i>
GO:0003729	MRNA Binding	1.000	<i>SRSF5</i>
GO:0005102	Receptor Binding	1.000	<i>AMN</i>
GO:0045296	Cadherin Binding	1.000	<i>CDH13</i>
GO:0090555	Phosphatidylethanolamine-Translocating ATPase Activity	1.000	<i>ATP8A2</i>
GO:0008273	Calcium, Potassium: Sodium Antiporter Activity	1.000	<i>SLC24A2</i>
GO:0005516	Calmodulin Binding	1.000	<i>SLC8A3</i>
GO:0000978	RNA Polymerase II Core Promoter Proximal Region Sequence-Specific DNA Binding	1.000	<i>ESRRB</i>
GO:0005262	Calcium Channel Activity	1.000	<i>SLC24A2</i>
GO:0003723	RNA Binding	1.000	<i>SRSF5</i>
GO:0043539	Protein Serine/Threonine Kinase Activator Activity	1.000	<i>DAB2IP</i>
GO:0031996	Thioesterase Binding	1.000	<i>TRAF3</i>
GO:0003707	Steroid Hormone Receptor Activity	1.000	<i>ESRRB</i>
GO:0051721	Protein Phosphatase 2A Binding	1.000	<i>DAB2IP</i>
GO:0035591	Signaling Adaptor Activity	1.000	<i>DAB2IP</i>

¹⁰GO-ID = Gene Ontology Identification Number

¹¹Gene(s) Assoc. = Genes linked to significant genetic variants in the metritis complex GWAS in-silico functional analysis

GO:0000287	Magnesium Ion Binding	1.000	ATP8A2
GO:0090556	Phosphatidylserine-Translocating ATPase Activity	1.000	ATP8A2
GO:0016887	ATPase Activity	1.000	ATP8A2
GO:0005496	Steroid Binding	1.000	ESRRB
GO:0019903	Protein Phosphatase Binding	1.000	TRAF3
GO:0050661	NADP Binding	1.000	POR
GO:0017124	Sh3 Domain Binding	1.000	DAB2IP
GO:0008508	Bile Acid: Sodium Symporter Activity	1.000	SLC10A1
GO:0031435	Mitogen-Activated Protein Kinase Kinase Kinase Binding	1.000	DAB2IP
GO:0070004	Cysteine-Type Exopeptidase Activity	1.000	SCRN1
GO:0032266	Phosphatidylinositol-3-Phosphate Binding	1.000	DAB2IP
GO:0003958	NADPH-Hemoprotein Reductase Activity	1.000	POR
GO:0005164	Tumor Necrosis Factor Receptor Binding	1.000	TRAF3
GO:0043565	Sequence-Specific DNA Binding	1.000	ESRRB
GO:0070273	Phosphatidylinositol-4-Phosphate Binding	1.000	DAB2IP
GO:0050660	Flavin Adenine Dinucleotide Binding	1.000	POR
GO:0030169	Low-Density Lipoprotein Particle Binding	1.000	CDH13
GO:0003700	Transcription Factor Activity, Sequence-Specific DNA Binding	1.000	ESRRB
GO:0016805	Dipeptidase Activity	1.000	SCRN1
GO:0071889	14-3-3 Protein Binding	1.000	DAB2IP
GO:0031434	Mitogen-Activated Protein Kinase Kinase Binding	1.000	DAB2IP
GO:0046875	Ephrin Receptor Binding	1.000	SIPA1L1
GO:0030165	PDZ Domain Binding	1.000	CRIM1
GO:0005123	Death Receptor Binding	1.000	DAB2IP
GO:0010181	FMN Binding	1.000	POR
GO:0005520	Insulin-Like Growth Factor Binding	1.000	CRIM1
GO:0043184	Vascular Endothelial Growth Factor Receptor 2 Binding	1.000	DAB2IP
GO:0004867	Serine-Type Endopeptidase Inhibitor Activity	1.000	CRIM1
GO:0044877	Macromolecular Complex Binding	1.000	DAB2IP
GO:0005432	Calcium: Sodium Antiporter Activity	1.000	SLC8A3
GO:0005509	Calcium Ion Binding	1.000	CDH13
GO:0016491	Oxidoreductase Activity	1.000	POR

GO:0036312	Phosphatidylinositol 3-Kinase Regulatory Subunit Binding	1.000	<i>DAB2IP</i>
GO:0055100	Adiponectin Binding	1.000	<i>CDH13</i>
GO:0061630	Ubiquitin Protein Ligase Activity	1.000	<i>RNF122</i>

Table S5. Enriched Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways for the metritis complex in Jersey and Holstein dairy cattle.

Pathway ID ¹²	Term	p-value	Gene(s) Assoc. ¹³
bta04668	TNF Signaling Pathway	0.117	<i>DAB2IP, TRAF3</i>
bta05161	Hepatitis B	0.163	<i>SLC10A1, TRAF3</i>
bta05168	Herpes Simplex Virus 1 Infection	0.346	<i>SRSF5, TRAF3</i>
bta04144	Endocytosis	1.000	<i>WIPF3</i>
bta04064	NF-KappaB Signaling Pathway	1.000	<i>TRAF3</i>
bta05412	Arrhythmogenic Right Ventricular Cardiomyopathy	1.000	<i>SLC8A3</i>
bta05160	Hepatitis C	1.000	<i>TRAF3</i>
bta04978	Mineral Absorption	1.000	<i>SLC8A3</i>
bta04620	Toll-Like Receptor Signaling Pathway	1.000	<i>TRAF3</i>
bta04714	Thermogenesis	1.000	<i>COX16</i>
bta04260	Cardiac Muscle Contraction	1.000	<i>SLC8A3</i>
bta04210	Apoptosis	1.000	<i>DAB2IP</i>
bta05165	Human Papillomavirus Infection	1.000	<i>TRAF3</i>
bta04622	Rig-I-Like Receptor Signaling Pathway	1.000	<i>TRAF3</i>
bta04020	Calcium Signaling Pathway	1.000	<i>SLC8A3</i>
bta05162	Measles	1.000	<i>TRAF3</i>
bta05200	Pathways In Cancer	1.000	<i>TRAF3</i>
bta04550	Signaling Pathways Regulating Plurip- otency of Stem Cells	1.000	<i>ESRRB</i>
bta04976	Bile Secretion	1.000	<i>SLC10A1</i>
bta04621	Nod-Like Receptor Signaling Pathway	1.000	<i>TRAF3</i>
bta04022	cGMP-Pkg Signaling Pathway	1.000	<i>SLC8A3</i>
bta04740	Olfactory Transduction	1.000	<i>SLC8A3</i>

¹² Pathway ID = KEGG Pathway Identification Number

¹³ Gene(s) Assoc. = Genes linked to significant genetic variants in the metritis complex GWAS in-silico functional analysis

bta05164	Influenza A	1.000	<i>TRAF3</i>
bta04974	Protein Digestion and Absorption	1.000	<i>SLC8A3</i>
bta04261	Adrenergic Signaling in Cardiomyocytes	1.000	<i>SLC8A3</i>
bta04371	Apelin Signaling Pathway	1.000	<i>SLC8A3</i>
bta05171	Coronavirus Disease - Covid-19	1.000	<i>TRAF3</i>
bta05222	Small Cell Lung Cancer	1.000	<i>TRAF3</i>
bta03040	Spliceosome	1.000	<i>SRSF5</i>
bta04150	mTOR Signaling Pathway	1.000	<i>DEPDC5</i>
bta05417	Lipid and Atherosclerosis	1.000	<i>TRAF3</i>
bta04657	Il-17 Signaling Pathway	1.000	<i>TRAF3</i>
bta05410	Hypertrophic Cardiomyopathy	1.000	<i>SLC8A3</i>
bta05414	Dilated Cardiomyopathy	1.000	<i>SLC8A3</i>
bta05135	Yersinia Infection	1.000	<i>WIPF3</i>
bta04015	Rap1 Signaling Pathway	1.000	<i>SIPA1L1</i>
bta05169	Epstein-Barr Virus Infection	1.000	<i>TRAF3</i>
bta05203	Viral Carcinogenesis	1.000	<i>TRAF3</i>
bta04936	Alcoholic Liver Disease	1.000	<i>TRAF3</i>
bta04961	Endocrine and Other Factor-Regulated Calcium Reabsorption	1.000	<i>SLC8A3</i>
bta05167	Kaposi Sarcoma-Associated Herpesvirus Infection	1.000	<i>TRAF3</i>