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Supplementary Materials: Comparative Transcriptomic Profiling and Gene Expression for Myxomatous Mitral Valve Disease in the Dog and Human

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Table 1. Comparison of gene fold changes in human MMVD (Thalji et al 2015 [2]; 2602 differentially expressed genes) with the 591 genes reported in the dog by Lu et al 2015 [1]. Both studies used the same FDR and fold settings, but Lu et al also use signal intensity to derive a much smaller gene set from an original set of 5397 differentially expressed genes. Only 109 differentially expressed genes were reported in both data sets of which 51 showed the same direction of fold change (+ or −) and 58 had the opposite fold change. The data illustrates that while there are similarities, there are also clear difference between human and canine MMVD the transcriptomic level.

	Lu et al 2015 Dog	Thaji et al 2015 Human
Gene Name	**Fold Change**	**Fold Change**
Acyl−CoA synthetase long-chain family member 5	2.09	−2.587
ADAMTS19	−5.27	1.76
Activating transcription factor 7	−2.104	−5.16
Angiopoietin 1	2.29	−1.46
Aryl hydrocarbon receptor nuclear translocator-like 2	1.57	1.808
ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	−5.22	−3.77
ATPase, class V, type 10A	−4.913	−3.61
ATPase, Na+/K+ transporting, alpha 3 polypeptide	−12.988	−3.53
Autism susceptibility candidate 2	1.588	−3.53
B-cell CLL/lymphoma 6, member B	−2.066	−3.32
B-cell linker	1.55	3.206
Bromodomain adjacent to zinc finger domain, 2A	−1.562	−3.24
Calpain, small subunit 1	−13.422	−3.22
Carbohydrate (chondroitin 4) sulfotransferase 11	2.17	−1.631
Carbonyl reductase 1	1.872	−3.17
Casein kinase 2, beta polypeptide	−1.757	−3.09
Caspase 8, apoptosis-related cysteine peptidase	3.98	1.844
Caspase recruitment domain family, member 6	1.73	−1.832
Cat eye syndrome chromosome region, candidate 1	1.73	−1.684
CDKN2A interacting protein	1.51	3.624
Cell growth regulator with EF-hand domain 1	3.55	1.636
Chemokine ligand 14	2.13	−6.419
Chemokine ligand 5	2.39	−2.706
Chemokine receptor 1	2.62	7.475
Coagulation factor C homolog, cochlin	2.34	−1.631
Complement factor I	2.79	2.479
Cold shock domain protein A	−2.85	−1.636
Cyclin−dependent kinase inhibitor 1A	2.84	−1.952
Cytochrome P450, family 4, subfamily B, polypeptide 1	3.51	−30.142
Destrin	2.9	−2.401

EPH receptor A3	2.31	1.671
Eukaryotic translation initiation factor 1 (EIF1)	−2.49	−4.47
Extracellular matrix protein 1	−2.47	3.148
Family with sequence similarity 171, member A1	−2.47	1.88
FAT tumor suppressor homolog 4 (Drosophila)	−2.44	1.788
Fc fragment of IgG, high affinity Ia, receptor, CD64	1.53	3.11
FRAS1 related extracellular matrix 1	−2.42	2.034
Fraser syndrome 1	−2.42	2.322
Frizzled-related protein	3.19	1.719
Fucosidase, alpha-L- 2, plasma	3.68	1.668
G protein-coupled receptor 126	2.2	−2.815
GABA(A) receptor−associated protein like 1	3.15	−2.815
General transcription factor IIA, 2, 12kDa	2.27	2.891
HIG1 domain family member 1A-like	−1.677	2.29
Homeodomain interacting protein kinase 2	−2.33	−3.512
Hydroxysteroid dehydrogenase 11	2.2	2.497
Hypoxia inducible factor 3, alpha subunit	−2.32	−1.508
Intraflagellar transport 172 homolog (Chlamydomonas)	−2.28	1.698
Janus kinase 2	2.24	−3.243
KIAA0430 ortholog	−2.27	1.601
LIM domain only 2 (rhombotin-like 1)	2.09	−2.283
Lysophosphatidylcholine acyltransferase 4	−2.22	1.564
Mastermind-like domain containing 1	−2.22	1.818
Matrix metallopeptidase 16	−2.22	4.045
Musculoskeletal, embryonic nuclear protein 1	2.2	−208.066
Myotubularin related protein 11	−2.13	1.918
Myosin heavy chain 11	2.71	−33.342
Nucleoporin	1.6	−1.904
Neuron navigator 2	−2.12	−2.488
Neuronal PAS domain protein 2	−2.12	−2.295
Nidogen 1	−2.2	−2.627
Nuclear factor of activated T-cells, calcineurin-dependent 1	−2.11	1.6
Odd-skipped related 1 (Drosophila)	2.09	3.509
Pallidin homolog (mouse)	5.39	−2.091
Period homolog 2 (Drosophila)	−2.08	1.52
Phosphoglucomutase 2	2.13	1.696
Phosphoinositide-3-kinase adaptor protein 1	2.9	−2.096
Phospholipase A2, group IVA	2.27	1.863
Phospholipase C-like 1	2.17	1.619
Phosphoinositide-3-kinase, class 2, beta polypeptide	−2.08	1.964
Pleckstrin	3.36	2.597
Plexin C1	2.14	1.92
Plexin domain containing 1	2.07	4.113
Potassium voltage-gated channel, KQT-like subfamily, member 5	−2.06	−6.398
Procollagen C-endopeptidase enhancer 2	2.58	1.555
Programmed cell death 1 ligand 2	1.73	1.925
Proline-rich protein 3-like	−2.04	1.793
Prostaglandin-endoperoxide synthase 2	2.34	−20.874
Protein phosphatase 1, regulatory subunit 12B	−2.01	−15.561
Protein tyrosine phosphatase, non-receptor type 14	−2.01	−8.842
Protocadherin beta 6	−2.01	2.575
Purinergic receptor P2X, ligand-gated ion channel, 7	1.55	1.54

Ras interacting protein 1	−2.01	−2.561
Receptor (G protein-coupled) activity modifying protein 2	−2	−2.86
Ras-like protein family member 11A-like	3.66	−4.274
Regulator of G-protein signaling 2	3.35	−2.68
Retinoic acid receptor responder	2.48	−2.108
RNA binding protein with multiple splicing 2	−1.98	−4.83
S100 calcium binding protein A4	2.94	1.921
Serine/threonine kinase 17b	2.34	−3.616
Serpin peptidase inhibitor, clade E member 2	2.36	2.149
Splicing factor 3a, subunit 1	−1.74	−1.502
Sodium channel, voltage-gated, type I, beta subunit	2.14	1.522
Solute carrier family 4 (sodium bicarbonate cotransporter), member 4	−1.78	−10.816
SRY (sex determining region Y)-box 9	−1.74	1.59
Superoxide dismutase 2, mitochondrial	2.27	−2.138
Synaptotagmin XVII	−1.72	3.535
Syntrophin, beta 1	−1.7	1.767
Tenascin XB	−1.7	2.145
TAF9 RNA polymerase II, TATA box binding protein-associated factor	1.57	−1.54
Tensin like C1 domain containing phosphatase	−1.69	−1.785
Toll−like receptor 1	3.12	1.542
Transgelin, smooth muscle protein 22-α	2.02	−5.957
Translocation associated membrane protein 2	−1.65	2.462
Ubiquitin-conjugating enzyme E2 N-like	−1.56	−1.88
Zinc finger, MIZ-type containing 1	−1.51	1.558

Table 2. Examples of fold change for a selection of genes in human and canine MMVD, illustrating similar and dissimilar changes in both species. 0 = no report of gene change. The genes selected represent signalling pathways involved in cell differentiation, endothelial-to-mesenchymal transition, extra−cellular matrix and inflammation. Of particular note are the differences in genes associated with myofibroblast activation.

Gene Name	**Function**	**Human (Thalji et al 2015) [2] Fold Change**	**Dog (Lu et al 2015) [1] Fold Change**
ACTA2; αSMA	Marker of myofibroblast formation	−3.945	10.66
ACTG2	smooth muscle actin found in enteric tissues	−99.8	15.35
IL-18	Proinflammatory cytokine	0	6.92
IL-6	Pro-inflammatory cytokine and an anti-inflammatory myokine	−16.9	7.86
IL-6R	Interleukin-6 receptor	−2.39	0
MYH-11; Myosin heavy chain 11	A heavy smooth muscle myosin	−33.3	4.93
CDH5; VE-cadherin	Calcium dependent cell adhesion molecule	−2.442	−2.559
TLR4	Pattern recognition receptor	0	2.35
Nid1; Nidogen 1	Basement membrane	−2.627	−3.08
Notch1	Developmental signalling	0	−2.33
Lama2; Laminin 2	Basement membrane	0	−5.15
CTSS; CathepsinS	Lysosomal enzyme and elastase	0	2.2

TAGLN; Transgelin	Shape-change sensitive actin	−5.957	2.39
FN; Fibronectin	Integrin associated glycoprotein	4.5	0
SNAIl	EMT/EndoMT associated transcription factor	0	4.8
BMP6	TGFβ superfamily signalling	0	2.38
HAS2;	Pro-migratory	2.497	2.18
RBPJ	NOTCH1 associated protein	0	1.6
NFATc1	Immune response transcription factor	1.6	−1.87
NFATc2	Immune response transcription factor	0	−2.13
PECAM-1; (CD31)	Endothelial cell-cell junction protein	−3.998	0

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