



## **Supplemental Material to:**

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**Gene expression alterations in rocky mountain  
elk infected with chronic wasting disease**

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**Box 1: Differentially expressed genes associated with CWD in Elk. These genes have not been reported to be associated to TSE disease in previous studies.**

Acyloxyacyl hydrolase; Angiopoietin 1; Angiotensin II receptor; ATPase, H<sup>+</sup> transporting, lysosomal 42kDa; Baculoviral IAP repeat-containing 3; Cadherin 18, type 2; Calcyon neuron-specific vesicular protein; Caldesmon 1; Calponin 1; Carboxypeptidase E; Cathelicidin; Caveolin 1; CD163 molecule; CDC28 protein kinase regulatory subunit 2; Ceruloplasmin; Chimerin 1; Cholecystokinin; Common salivary protein BSP30; Complement component 4A; Complement factor B and H; Connective tissue growth factor CTD; Cyclin-dependent kinase inhibitor 1C; Cysteine and glycine-rich protein; Cysteine-rich, angiogenic inducer; Cytokeratin 19; Deleted in malignant brain tumors 1; Destrin; Elongation factor RNA polymerase II; Ermin; Fatty acid binding protein 4; Fibroblast growth factor 12; Fibroblast growth factor-binding protein; Frizzled-related protein; GDP dissociation inhibitor 1; GINS complex subunit 4; GNAS complex locus; Growth hormone receptor; GTP-binding protein 8; Haptoglobin; Heme oxygenase 1; Hemoglobin alpha chain Fc fragment of IgG; Hemoglobin, beta; Intersectin 1; IQ motif containing GTPase activating protein 1; Kv channel interacting protein 4; Mal, T-cell differentiation protein 2; Meiotic nuclear divisions 1 homolog; Microsomal glutathione S-transferase 1; Microtubule-associated protein 1B; Myocilin; Myotilin; NECAP endocytosis associated 2; Neurensin 1; Neurocalcin delta; Neurofilament, heavy polypeptide 200kDa; Neuron specific gene family member 1; Neuropilin 1; Neurotrimin; NHP2 non-histone chromosome protein 2-like 1; Nuclear receptor subfamily 3; Nuclear receptor subfamily 4; Polymerase (RNA) II polypeptide A; Prosaposin Protein-L-isoaspartate O-methyltransferase; RAB2A, member RAS oncogene family; Radixin; Rho GTPase activating protein 29; Rho-associated, coiled-coil containing protein kinase 2; RING1 and YY1 binding protein; RNA binding motif protein 3; RNA-binding region (RNP1, RRM) containing 3; Scinderin; Serum amyloid A-like; SH3 domain binding glutamic acid-rich protein like 3; Similar to Chain D, Crystal Structure Of The Adenylyl Cyclase Domain Of Anthrax Edema Factor In Complex With Calmodulin; Similar to EBF1 protein; Similar to HMGB2 protein; Similar to Kinesin-like protein KIF3A; Similar to macrophage receptor MARCO; Similar to RIKEN cDNA 1110064P04 gene; Spi-C transcription factor; Stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein) TAF9 RNA polymerase II; Tax1 binding protein 1; Tensin 3; Tetratricopeptide repeat domain 35; Topoisomerase (DNA) II alpha 170kDa; Transmembrane protein 55; TRIM6-TRIM34; Troponin C type 2; Ubiquitin carboxyl-terminal esterase L1; Voltage-dependent anion channel 1; Von Ebner minor salivary gland protein and Zinc finger protein 618.

Table S1- Gene Ontology (GO) analysis of Differentially expressed genes using GeneSifter for biological processes, cellular component and molecular function in different tissues from Chronic wastings disease infected and control brain and gut tissues of ELK.

Brain					Midbrain					Thalamus				
Ontology	Genes	GO	List	z-score	Ontology	Genes	GO	List	z-score	Ontology	Genes	GO	List	z-score
cellular process	50	17	33	3929 -1.7 1.64	cellular process	13	6	7	3929 -3 0.47	cellular process	43	6	37	3929 -3.21 0.53
biological regulation	32	12	20	1920 0.86 1.97	biological regulation	10	7	3	1920 -1 -0.12	metabolic process	28	8	20	3035 -0.08 -2.36
metabolic process	31	14	17	3035 -0.7 -1.9	localization	9	6	3	1161 2 0.9	localization	25	4	21	1161 0.58 3.72
regulation of biological process	29	11	18	1764 0.8 1.71	regulation of biological process	9	7	2	1764 2 -0.67	biological regulation	24	7	17	1920 1.05 -0.13
localization	20	9	11	1161 1.42 0.93	establishment of localization	7	5	2	1015 2 0.28	establishment of localization	21	3	18	1015 0.19 3.27
multicellular organismal process	20	6	14	987 0.45 2.77	immune system process	7	5	2	347 5 1.96	multicellular organismal process	20	4	16	987 0.93 2.65
signaling	17	2	15	976 -1.5 3.24	metabolic process	7	3	4	3035 -3 -0.73	response to stimulus	20	8	12	851 4.18 1.7
cellular component organization	16	6	10	720 1.29 2.19	positive regulation of biological process	7	5	2	595 3 1.1	regulation of biological process	19	7	12	1764 1.31 -1.26
establishment of localization	16	8	8	1015 1.36 0.19	response to stimulus	7	5	2	851 2 0.55	negative regulation of biological process	13	6	7	595 3.73 0.74
response to stimulus	16	8	8	851 1.91 0.74	developmental process	6	3	3	779 1 1.65	signaling	13	1	12	976 -1.12 1.19
developmental process	15	5	10	779 0.54 1.92	multicellular organismal process	6	3	3	987 0 1.21	developmental process	12	3	9	779 0.69 0.8
signaling process	14	2	12	643 -0.8 3.57	cellular component organization	5	3	2	720 1 0.81	cellular component organization	11	2	9	720 0.06 1.05
positive regulation of biological process	13	5	8	595 1.18 1.83	negative regulation of biological process	3	2	1	510 1 0.18	immune system process	11	5	6	347 4.39 1.68
negative regulation of biological process	12	3	9	510 0.24 2.84	cell proliferation	2	1	1	290 0 0.78	negative regulation of biological process	11	3	8	510 1.48 1.67
cellular component biogenesis	8	3	5	320 1.09 1.77	cellular component biogenesis	2	2	0	320 0 -0.75	signaling process	9	1	8	643 -0.59 0.97
immune system process	8	4	4	347 1.72 0.92	death	2	1	1	322 0 0.67	cellular component biogenesis	6	1	5	320 0.16 1.28
cell proliferation	7	3	4	290 1.27 1.3	locomotion	2	1	1	174 1 1.36	locomotion	6	2	4	174 2.29 1.97
death	7	1	6	322 -0.5 2.43	signaling	2	0	2	976 -2 0.34	cell proliferation	5	1	4	290 0.26 0.87
biological adhesion	5	2	3	211 -0.9 1.18	signaling process	2	0	2	643 -1 0.98	biological adhesion	4	0	4	211 -0.24 -0.44
locomotion	5	2	3	174 1.19 1.54	biological adhesion	1	1	0	211 1 -0.6	death	4	0	4	322 -0.96 0.66
rhythmic process	3	1	2	20 2.81 4.83	growth	1	0	1	152 -1 1.52	growth	2	0	2	152 -0.65 0.54
growth	2	1	1	152 0.25 -0.1	multi-organism process	1	0	1	127 -1 1.75	multi-organism process	1	0	1	127 -0.59 -0.14
multi-organism process	2	0	2	127 -0.8 1.11	pigmentation	1	0	1	17 -0 5.82	rhythmic process	1	0	1	20 -0.23 1.93
reproduction	2	0	2	164 -0.9 0.72	reproduction	1	0	1	164 -1 1.43	carbon utilization	0	0	0	1 -0.05 -0.1
reproductive process	2	0	2	162 -0.9 0.74	reproductive process	1	0	1	643 -1 0.44	cell killing	0	0	0	21 -0.24 -0.44
pigmentation	1	0	1	17 -0.3 2.47	rhythmic process	1	0	1	20 -0 5.34	cell wall organization or biogenesis	0	0	0	8 -0.15 -0.27
carbon utilization	0	0	0	1 -0.1 -0.1	carbon utilization	0	0	0	1 -0 -0.04	nitrogen utilization	0	0	0	1 -0.05 -0.1
cell killing	0	0	0	21 -0.3 -0.4	cell killing	0	0	0	21 -0 -0.19	pigmentation	0	0	0	17 -0.21 -0.4
cell wall organization or biogenesis	0	0	0	8 -0.2 -0.2	cell wall organization or biogenesis	0	0	0	8 -0 -0.12	reproduction	0	0	0	164 -0.68 -1.25
nitrogen utilization	0	0	0	1 -0.1 -0.1	nitrogen utilization	0	0	0	1 -0 -0.04	reproductive process	0	0	0	162 -0.67 -1.24
viral reproduction	0	0	0	14 -0.3 -0.3	viral reproduction	0	0	0	14 -0 -0.15	viral reproduction	0	0	0	14 -0.19 -0.36

Spleen

Spleen					Tonsil					RPLN							
Ontology	Totals	Genes	GO	List	z-score	Ontology	Totals	Genes	GO	List	z-score	Ontology	Totals	Genes	GO	List	z-score
cellular process	67	45	22	3929 -0.9 -0.7	response to stimulus	14	9	5	851 6 3	cellular process	7	7	0	3929 -0.25 -2.92			
metabolic process	42	30	12	3035 -1.9 -2.4	cellular process	12	5	7	3929 -3 -0.25	metabolic process	7	7	0	3035 0.94 -1.83			
biological regulation	37	25	12	1920 0.44 0.2	metabolic process	11	6	5	3035 -0 -0.43	response to stimulus	6	4	2	851 2.12 3.07			
regulation of biological process	35	23	12	1764 0.42 0.56	biological regulation	7	3	4	1920 -1 0.3	biological regulation	5	4	1	1920 0.3 3.0			
response to stimulus	35	26	9	851 5.39 1.92	regulation of biological process	7	3	4	1764 -0 0.5	regulation of biological process	5	4	1	1764 0.5 0.4			
multicellular organismal process	29	18	11	987 1.95 2.36	immune system process	6	3	3	347 3 2.05	locomotion	3	2	1	174 3.01 3.53			
cellular component organization	21	14	7	720 1.93 1.41	localization	5	1	4	1161 -1 1.44	multicellular organismal process	3	3	0	987 0.97 -0.71			
localization	21	10	11	1161 -1.3 1.77	multicellular organismal process	5	3	2	987 1 0.14	signaling	3	3	0	976 0.99 -0.71			
developmental process	20	11	9	779 0.54 2.2	positive regulation of biological process	5	3	2	595 2 0.91	biological adhesion	2	2	0	211 2.63 -0.3			
signaling	17	6	11	976 -1.9 2.4	cellular component organization	3	1	2	720 -0 0.62	developmental process	2	2	0	779 0.5 -0.62			
positive regulation of biological process	15	9	6	595 0.7 1.39	developmental process	3	2	1	779 0 -0.4	growth	2	2	0	152 3.29 -0.25			
establishment of localization	14	5	9	1015 -2.4 1.34	locomotion	3	1	2	174 1 3.01	immune system process	2	0	2	347 -0.83 5.1			
immune system process	13	13	0	347 4.46 -1.5	multi-organism process	3	0	3	127 -1 5.78	localization	2	2	0	1161 -0.12 -0.79			
negative regulation of biological process	11	9	2	510 1.19 -0.6	biological adhesion	2	1	1	211 1 1	negative regulation of biological process	2	1	1	510 0.06 1.82			
signaling process	11	3	8	643 -1.9 2.28	cell wall organization or biogenesis	2	0	2	8 -0 16.32	reproduction	2	1	1	164 1.28 3.65			
locomotion	10	7	3	174 3.44 1.96	death	2	0	2	322 -1 1.88	reproductive process	2	1	1	162 1.3 3.67			
cell proliferation	9	6	3	290 1.37 0.99	establishment of localization	2	0	2	1015 -2 0.1	cellular component organization	1	1	0	720 -0.32 -0.59			
death	8	7	1	322 1.62 -0.7	reproduction	2	1	1	164 1 1.28	positive regulation of biological process	1	1	0	595 -0.11 -0.53			
multi-organism process	7	4	3	127 2.01 2.61	reproductive process	2	1	1	162 1 1.3	viral reproduction	1	0	1	14 -0.16 13.1			
cellular component biogenesis	6	5	1	320 0.58 -0.7	signaling	2	1	1	976 -1 -0.67	carbon utilization	0	0	0	1 -0.04 -0.02			
reproduction	5	4	1	164 1.45 0.02	cellular component biogenesis	1	0	1	320 -1 0.55	cell killing	0	0	0	21 -0.2 -0.09			
reproductive process	5	4	1	162 1.48 0.03	growth	1	1	0	152 1 -0.54	cell proliferation	0	0	0	290 -0.76 -0.36			
cell wall organization or biogenesis	3	3	0	8 9.37 -0.2	negative regulation of biological process	1	0	1	510 -1 0.06	cell wall organization or biogenesis	0	0	0	8 -0.12 -0.06			
growth	3	1	2	152 -0.6 1.17	signaling process	1	0	1	643 -1 -0.19	cellular component biogenesis	0	0	0	320 -0.8 -0.38			
biological adhesion	2	1	1	211 -1 -0.2	viral reproduction	1	0	1	14 -0 6.06	death	0	0	0	322 -0.8 -0.38			
cell killing	1	0	1	21 -0.5 2.48	carbon utilization	0	0	0	1 -0 -0.04	establishment of localization	0	0	0	1015 -1.54 -0.73			
carbon utilization	0	0	0	1 -0.1 -0.1	cell killing	0	0	0	21 -0 -0.2	multi-organism process	0	0	0	127 -0.49 -0.23			
nitrogen utilization	0	0	0	1 -0.1 -0.1	cell proliferation	0	0	0	290 -1 -0.76	nitrogen utilization	0	0	0	1 -0.04 -0.02			
pigmentation	0	0	0	17 -0.5 -0.3	nitrogen utilization	0	0	0	1 -0 -0.04	pigmentation	0	0	0	17 -0.18 -0.08			
rhythmic process	0	0	0	20 -0.5 -0.4	pigmentation	0	0	0	17 -0 -0.18	rhythmic process	0	0	0	20 -0.19 -0.09			
viral reproduction	0	0	0	14 -0.4 -0.3	rhythmic process	0	0	0	20 -0 -0.19	signaling process	0	0	0	643 -1.17 -0.55			

**Table S2 - Summary of Ingenuity networks generated by mapping of differentially expressed genes identified from Chronic wastings disease infected and control brain and gut tissues of Elk.**

Brain	Genes in Network	Score	Focus Genes	Top Functions
1	26s Proteasome, Actin, Calmodulin, CAPZA2, CDKN1C, CS, ERMN, F Actin, GD11, GNAS, GPNMB, Histone h3, ID2, LCP1, MAG, MAPK3, MT1F, NEFH, NEFM, NRAA2, NTM, PCP4, POLR2A, PRPH, RDX, Rho gdi, RHOB, SCIN, SDCBP, SNAP25, SNCA, SOD1, TAC1, TAX1BP1, Tubulin	67	28	Neurological Disease, Cell Morphology, Cellular Assembly and Organization
2	ATAD2, ATP, CDKN2A, CEBPB, CTRP, CTRAT, CXCL2, FGF7, GNAI1, GNAI3, GPD1, GPSM3, HNF4A, HP, KCN12, KIT, MAP3K3, MAPK8, OGFOD2, PCP2, PEPO, PLEKH8, PLOD1, PPARG, PROZ, PTPLAD1, RAB2A, SORL1 (includes EG:58472), SYT4, TBRG1, TCF19, TMEM176A, TMEM176B, TTR	24	13	Cell Cycle, Genetic Disorder, Cancer
3	ASC2, C3AR1, CALCB (includes EG:797), CALCRL, CD68, COL11A1, COL24A1, COL8A2, CTSH, EGR2, EVI2A, EVX1, FEZ2, FOS, GPR18, HOXA9, JUN, MT1A, NBP1, PCDHGC3, PCNX, PPA1, PTGDS, RCHY1, RGS1, SATB1, SCN3B, SULF2, TAOK1, TLN2, TMSB10, TP53, TP53AIP1, YY2 (includes EG:404281), ZFP36L1	21	12	Cell Cycle, Gene Expression, Cell Death
4	Basal transcriptional machinery, Cbp/p300-Hd-Taf4-Taf9b-Tbg, COT6B, CHN1 (includes EG:1123), CHN1, CPNE5, CREBBP, CRYGF, CYR61, EBF1, EDN1, EID1, EP300, ERBB2, HTT, Irf alpha/beta, LSAMP, Mediator, MOG, N4BP2, NPTN, NTM, OPCML, p160, p300-CBP, PRNP, RETN, RNPC3, SEPT7, SH3BGR1, SS18L1, STRN, TGS1, TIF2-NCOA1-p300-PCAF-CBP, TRERF1	19	11	Cellular Function and Maintenance, Neurological Disease, Cancer
5	ABCC1, AEBP2, ATP2A1, BRD8, BRWD1, Ca2+, CDH11, EEF2, H3F3A (includes EG:3020), HBG1, HLTf, HRC, IKZF3, JARID2, JPH1, LCAT, MI2, MKL1, MORC3, MTF2, MYCN, MYH7, RBBP4, RCOR1, RFC3, RPS15, SERPINH1, SETX, SMARCA4, SP3, SPARC, STK38, TAGLN, TRIM35, VSNL1	13	8	Cell Cycle, Cellular Assembly and Organization, DNA Replication, Recombination, and Repair
<b>Midbrain</b>				
1	CALCRL, Calmodulin, CEBPB, COL1A1, CP, CTSH, EDNRB, Gpcr, GPR55, GPR84, GPR113, GPR120, GPR144, GPR173, GPR174, GPR176, GPR89A, GPR89C, GPRC6A, GRK5, GSTA1, HLA-DRA, HLA-DRB1, HSPD1, HTT, ITGA11, LCP1, LGR4, LPAR6, OPN1MW2, SCN3B, SEPT7, TAA8, TP53, VN1B3	26	11	Neurological Disease, Cell Death, Organismal Survival
2	A2M, AQP4, ARG2, ARHGEF40, ATP6V1D, C11ORF51, C11ORF58, CCDC25, CD68, CYP2J2, DMD, GAS1, GSS, HNF4A, IFI30, IFITM2, JUN, KCN12, LOC729991-MEF2B, MAL2, MAP3K3, MAP3K13, MGST1, MGST2, MGST3, MIRLET7B (includes EG:406884), MT1F, MTF1, REG1B, SCIN, SLC39A9, SMAD2, SOD1, STAT3, ZNHIT6	24	10	Hepatic System Disease, Liver Cholestasis, Gene Expression
<b>Thalamus</b>				
1	A2M, Beta Tubulin, Calmodulin, Calmodulin-Ca2+-CaMKII+Calmodulin-Ca2+, Calmodulin-CaMKII-Ca2+, Calmodulin-CaMKII-Ca2+, CAMK2B, CCK, CXCL2, FCRL6, GAP43, GAPDH (includes EG:2597), HLA-DRA, HLA-DRB1, MAP6, N-cor, NCALD, NFkB (complex), NHP2L1, NTM, PCP4, Pgc, PGK1, SNAP25, SNAP91, SNCA, STMN2, TAC1, TAF9, THY1, TUBB4Q, Tubulin, UCHL1, VDAC1, ZDHHC7	49	22	Genetic Disorder, Neurological Disease, Psychological Disorders
2	ABCC6, ATL1, C16ORF80, C3ORF34, CHMP1B, DAD1, FKBP10, FKBP1B, GINS2, GINS4, HNF4A, HNF4a dimer, MDH1, MDH2, NAT8, NDUFB5, PCMT1, PGAM1, PPARGC1A, PPL1, PPL2, PPP1CA, PPP1R1, PPP1R14D, PPP1R15B, PPP1R3B, PVALB, RAB33B, SLC25A20, SLC26A11, SPAST, STT3A, TGFBR1, TUSC3, WDR13	20	11	Gene Expression, Energy Production, Small Molecule Biochemistry
3	ADRB2, AVP, CD68, CTSH, FOS, GFIB, GNB5, Gpcr, GPR55, GPR84, GPR113, GPR120, GPR144, GPR173, GPR174, GPR176, GPR89A, GPR89C, GPRC6A, IKBKG, JUN, KIFAP3, LGR4, LPAR6, MAPK10, NELL2, NTS, OPN1MW2, SEKN1, SRC, TAA8, TAF1, VN1B2, VN1B3, VSNL1	18	10	Cancer, Gene Expression, Genetic Disorder
4	ANGPTL4, ATP1B1, ATP6V1C1, ATP6V1C2, AXIN2, BHLHE41, CA9, CHD8, CP, CTNNB1, EDN1, EDN3, Endothelin, FOXP3, HIF1A, HP, KCNIP4, LPIN1, MB, MIR122 (includes EG:406906), MPO, NAA10, nitric oxide, NRN1, NT5E, p160, PPARG, RGS1, SCD, SCG2, SMAD7, TGFB3, TNF, TTR	16	10	Organismal Injury and Abnormalities, Cellular Development, Connective Tissue Development and Function
<b>Spleen</b>				
1	A2M, Ap1, APP, BLNK, CAMP, CCNB1, CD69, CENPF, CFB, CKM, FABP4, HBB (includes EG:3043), Histone h3, Histone h4, HMGN1, HP, Hsp70, JUN, KIAA0101, KRT19, Laminin, MIF, MME, Mmp, MMP7, NCAPG (includes EG:64151), NFkB (complex), PCNA, RNA polymerase II, RRM2, SAA1, SMC4, SPP1, TOP2A, Ubiquitin	51	26	Cancer, Reproductive System Disease, Cell Death
2	ACTG2 (includes EG:72), Actin, ALKBH8, BASP1, CALD1, Calmodulin, CAPZA2, CCL2, CCL20, CHEMOKINE, CXCL10, CXCL14, CXCR4, DNAJB1, Estrogen Receptor, F Actin, Hsp90, HSP90AA1, HSPA8, IQGAP1, MAP1B, Mic, MYH8, MYH10, MYL1, Myosin, ROCK2, S100A9, SHCBP1, SPA17, SPTA1, SPTB1, STMN2, Tubb1	49	26	Cellular Movement, Hematological System Development and Function, Immune Cell Trafficking
3	ADH1C, AZGP1, BMP24, C20ORF114, CSR3, DES, EBF1, EGF, FGF6, FGFRL1, FLT4, GHR, GPNMB, growth factor receptor, H2-M1, IKBIP, KIF11, KIT, LTF, MYO1, NTRK2, PLC gamma, PLUNC, POSTN, PSAP, RXRA, SPIC, TAC1, TCF3, TCN1, TFE2, TGFBR3, TNFSE13B, TNNI2, WDR2	28	16	Cancer, Reproductive System Disease, Molecular Transport
4	AGTR1, AKT1, ARHGAP15, ARHGAP29, ARHGAP10, ARRB2, BIRC3, CASP3, CASP3/67, CFI, CHN2, Ciap, COX7A2L, ELOVL1, FPR1, HTR2B, KCNAB1, MGST3, MIR124, NDRG2, NECAP2, ONECUT1, PIK3R1, RGS13, RPL28, RPS6KB2, RRH, SLC1A3, SLC25A13, SNCA, SNCB, TGFBR1, TMOC2, TP53, UBE2	21	13	Cell Death, Cancer, Cellular Movement
5	CK1, FBLN1, FLNA, FLNC, FRZB, FZD1, FZD3, FZD10, GPR39, GPR137, GPR146, GPR160, HMG1 (includes EG:3146), HNF4A, INHBE, LTB4R2, MAL2, MRPS18B, MYOC, MYOT, NUF2, OTUD1, P2RY14, PHLD2, PSAT1, RANBP1, RB1, RBAK, RBBP9, SGCB, SGCE, SLC22A18A5, UCHL1, VN1B1, WNT11	19	12	Cellular Assembly and Organization, Cancer, Cardiovascular System Development and Function
6	ANGPT1, ATXN1, BRCA1, BTAF1, CHRDL1, DIAPH3, DNAJA1, DNAJB3 (includes EG:414061), DNAJC2, DNAJC12, DNAJC22, DNAJC24, DNAJC25, DNAJC27, DNAJC28, DNAJC30, EAF2, ELL3, GBP2, GTF2F2L, HELLS, Holo RNA polymerase II, HSP, HSPA12A, HSPA12B, HSPB11, HSPH1, KLHL8, MIRLET7E (includes EG:406887), MYC, POLR2J2, POLR2L (includes EG:64491), SLMAP, TAF9B, TGF5A	18	11	Gene Expression, Infection Mechanism, Cell Cycle
7	AGR2, AK1, CACYBP, CTSH, DUT (includes EG:1854), EGFR, EMCN, FHL2, FOS, IL4, IL7, KBTBD10, MED31, MT1A, MUC2, MUC4, MUC6, MUC12 (includes EG:10071), MUC3A (includes EG:4584), MUC3A (includes EG:687030), MUC5AC, Mucin, MYBPC1, NUT2, PERP, PROL1 (includes EG:17830), RPS25, SCAMP1, SELENBP1, SIGLEC9, SPARCL1, TFF3, TMCO3, TP53, YY2 (includes EG:404281)	15	10	Cell Cycle, Cellular Development, Cellular Growth and Proliferation
<b>RPLN</b>				
1	CACYBP, CCL5, CDK6, CEBPA, CTGF, CTNNB1, CYR61, DNAJA1, DNAJB1, DNAJB7, DNAJB13, DNAJB3 (includes EG:414061), DNAJC2, DNAJC12, DNAJC15, DNAJC22, DNAJC24, DNAJC25, DNAJC27, DNAJC28, DNAJC30, DNAJC5B, FBXO7, FMR1, FOS, HLA-B, HP, HSP, HSPA12A, HSPA12B, HSPB11, HSPH1, KLRC1, RGS13, SP1	33	12	Infection Mechanism, Cellular Assembly and Organization, Organ Development
<b>Tonsil</b>				
1	C4BPA, CAPZA2, CCL21, CD163, CLTC, DNAJA1, DNAJB1, DNAJB7, DNAJB13, DNAJB3 (includes EG:414061), DNAJC2, DNAJC12, DNAJC22, DNAJC24, DNAJC25, DNAJC27, DNAJC28, DNAJC30, DNAJC5B, heparin, HSP, HSPA12A, HSPA12B, HSPB11, HSPH1, IL8, NFKBIA, PERP, PRKCA, RBX1 (includes EG:56438), S100A9, S100A12, SPRR3 (includes EG:6707), TP53, Ubiquitin	32	13	Infection Mechanism, Hematological Disease, Organismal Injury and Abnormalities
2	ASCB1, AKAP12, APPL1, AXIN2, C12ORF53, CBFA2T3, CIR1, CTNNB1, CXADR, CYR61, DKK1, FABP2, FABP4, FGF8P1, HDAC1, HDAC7, HDAC10, HESX1, IGF2BP2, INPP5A, INPP5K, LPIN1, MDF1 (includes EG:4188), MI2, MIR34C (includes EG:407042), MTA3, NCOR2, SALL1, SOX6, SOX17, SPEN, TBL1X, TFAP4, UHRE2, ZBTB7A	12	6	Cellular Development, Cellular Growth and Proliferation, Gene Expression

All the potential networks that scored > 9 are listed (a score of 3 or greater is considered significant with p<0.001).

**Table S3 - Major canonical pathways (top 5) over-represented by differentially expressed genes from Chronic wastings disease infected and control brain and gut tissues of Elk as determined using the Ingenuity Pathway Analysis.**

	<b>Ingenuity Canonical Pathways</b>	<b>-log(p-value)</b>	<b>Ratio</b>	<b>Molecules</b>
<b>Brain</b>				
	Amyotrophic Lateral Sclerosis Signaling	2.79E+00	3.39E-02	PRPH, SOD1, NEFM, NEFH
	Endothelin-1 Signaling	2.70E+00	2.60E-02	GNAS, LCAT, EDN1, MAPK3, GNAI1
	Androgen Signaling	2.57E+00	2.76E-02	GNAS, POLR2A, MAPK3, GNAI1
	Synaptic Long Term Depression	2.20E+00	2.45E-02	GNAS, LCAT, MAPK3, GNAI1
	CXCR4 Signaling	2.08E+00	2.34E-02	GNAS, RHOB, MAPK3, GNAI1
<b>Midbrain</b>				
	B Cell Development	2.83E+00	5.41E-02	HLA-DRA, HLA-DRB1
	Antigen Presentation Pathway	2.73E+00	4.65E-02	HLA-DRA, HLA-DRB1
	Graft-versus-Host Disease Signaling	2.61E+00	4.00E-02	HLA-DRA, HLA-DRB1
	Autoimmune Thyroid Disease Signaling	2.60E+00	3.28E-02	HLA-DRA, HLA-DRB1
	NRF2-mediated Oxidative Stress Resp	2.54E+00	1.56E-02	MGST1, SOD1, GSTA1
<b>Thalamus</b>				
	Parkinson's Signaling	2.63E+00	1.11E-01	UCHL1, SNCA
	OX40 Signaling Pathway	2.28E+00	3.12E-02	HLA-DRA, MAPK10, HLA-DRB1
	Acute Phase Response Signaling	2.27E+00	2.19E-02	TTR, HP, CP, A2M
	Crosstalk between Dendritic Cells and IL-6 Signaling	2.20E+00	3.06E-02	HLA-DRA, HLA-DRB1, CAMK2B
		2.19E+00	3.00E-02	MAPK10, CD14, A2M
<b>Spleen</b>				
	Hepatic Fibrosis / Hepatic Stellate Cell Activation	2.99E+00	4.08E-02	MYH10, CCL2, MYH8, A2M, MYL1, AGTR1
	Protein Ubiquitination Pathway	2.86E+00	2.92E-02	UCHL1, UBD, HSPA8, HSPH1, HSP90AA1, DNAJB1, DNAJA1, BIRC3
	Actin Cytoskeleton Signaling	2.73E+00	2.94E-02	ROCK2, MYH10, MYH8, DIAPH3, ACTG2 (includes EG:72), IQGAP1, MYL1
	Chemokine Signaling	2.56E+00	5.33E-02	ROCK2, JUN, CCL2, CXCR4
	Aldosterone Signaling in Epithelial Cells	2.05E+00	2.91E-02	HSPA8, HSPH1, HSP90AA1, DNAJB1, DNAJA1
<b>RPLN</b>				
	Aldosterone Signaling in Epithelial Cell	3.44E+00	1.74E-02	HSPH1, DNAJB1, DNAJA1
	Protein Ubiquitination Pathway	2.78E+00	1.09E-02	HSPH1, DNAJB1, DNAJA1
	IGF-1 Signaling	2.49E+00	2.00E-02	CTGF, CYR61
	Role of Tissue Factor in Cancer	2.33E+00	1.72E-02	CTGF, CYR61
	Hepatic Fibrosis / Hepatic Stellate Cell	2.14E+00	1.36E-02	CTGF, CCL5
<b>Tonsil</b>				
	Aldosterone Signaling in Epithelial Cell	2.84E+00	1.74E-02	HSPH1, DNAJB1, DNAJA1
	Protein Ubiquitination Pathway	2.20E+00	1.09E-02	HSPH1, DNAJB1, DNAJA1
	Role of Tissue Factor in Cancer	1.94E+00	1.72E-02	IL8, CYR61
	Airway Pathology in Chronic Obstructiv	1.93E+00	1.11E-01	IL8
	Hepatic Fibrosis / Hepatic Stellate Cell	1.75E+00	1.36E-02	IL8, CCL21

**Table S4. Differentially expressed genes associated with CWD in Elk. These genes have not been reported to be associated to TSE disease in previous studies.**

Acyloxyacyl hydrolase
Angiopoietin 1
Angiotensin II receptor
ATPase, H <sup>+</sup> transporting, lysosomal 42kDa
Baculoviral IAP repeat-containing 3
Cadherin 18, type 2
Calcyon neuron-specific vesicular protein
Caldesmon 1
Calponin 1
Carboxypeptidase E
Cathelicidin
Caveolin 1
CD163 molecule
CDC28 protein kinase regulatory subunit 2
Ceruloplasmin
Chimerin 1
Cholecystokinin
Common salivary protein BSP30
Complement component 4A
Complement factor B and H
Connective tissue growth factor CTD
Cyclin-dependent kinase inhibitor 1C
Cysteine and glycine-rich protein
Cysteine-rich, angiogenic inducer
Cytokeratin 19
Deleted in malignant brain tumors 1
Destrin
Elongation factor RNA polymerase II
Ermin
Fatty acid binding protein 4
Fibroblast growth factor 12
Fibroblast growth factor-binding protein
Frizzled-related protein
GDP dissociation inhibitor 1
GINS complex subunit 4
GNAS complex locus
Growth hormone receptor
GTP-binding protein 8
Haptoglobin
Heme oxygenase 1
Hemoglobin alpha chain Fc fragment of IgG
Hemoglobin, beta
Intersectin 1
IQ motif containing GTPase activating protein 1
Kv channel interacting protein 4
Mal, T-cell differentiation protein 2
Meiotic nuclear divisions 1 homolog
Microsomal glutathione S-transferase 1
Microtubule-associated protein 1B
Myocilin
Myotilin

NECAP endocytosis associated 2
Neurensin 1
Neurocalcin delta
Neurofilament, heavy polypeptide 200kDa
Neuron specific gene family member 1
Neuropilin 1
Neurotrimin
NHP2 non-histone chromosome protein 2-like 1
Nuclear receptor subfamily 3
Nuclear receptor subfamily 4
Polymerase (RNA) II polypeptide A
Prosaposin Protein-L-isoaspartate O-methyltransferase
RAB2A, member RAS oncogene family
Radixin
Rho GTPase activating protein 29
Rho-associated, coiled-coil containing protein kinase 2
RING1 and YY1 binding protein
RNA binding motif protein 3
RNA-binding region (RNP1, RRM) containing 3
Scinderin
Serum amyloid A-like
SH3 domain binding glutamic acid-rich protein like 3
Similar to Chain D, Crystal Structure Of The Adenylyl Cyclase Domain Of Anthrax Edema Factor In Complex With Calmodulin
Similar to EBF1 protein
Similar to HMGB2 protein
Similar to Kinesin-like protein KIF3A
Similar to macrophage receptor MARCO
Similar to RIKEN cDNA 1110064P04 gene
Spi-C transcription factor
Stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein) TAF9 RNA polymerase II
Tax1 binding protein 1
Tensin 3
Tetratricopeptide repeat domain 35
Topoisomerase (DNA) II alpha 170kDa
Transmembrane protein 55
TRIM6-TRIM34
Troponin C type 2
Ubiquitin carboxyl-terminal esterase L1
Voltage-dependent anion channel 1
Von Ebner minor salivary gland protein and Zinc finger protein 618