

Supplementary Figures

Unprocessed gel images/data files are available at <https://figshare.com/s/a7fe6149482d21aabf3a>

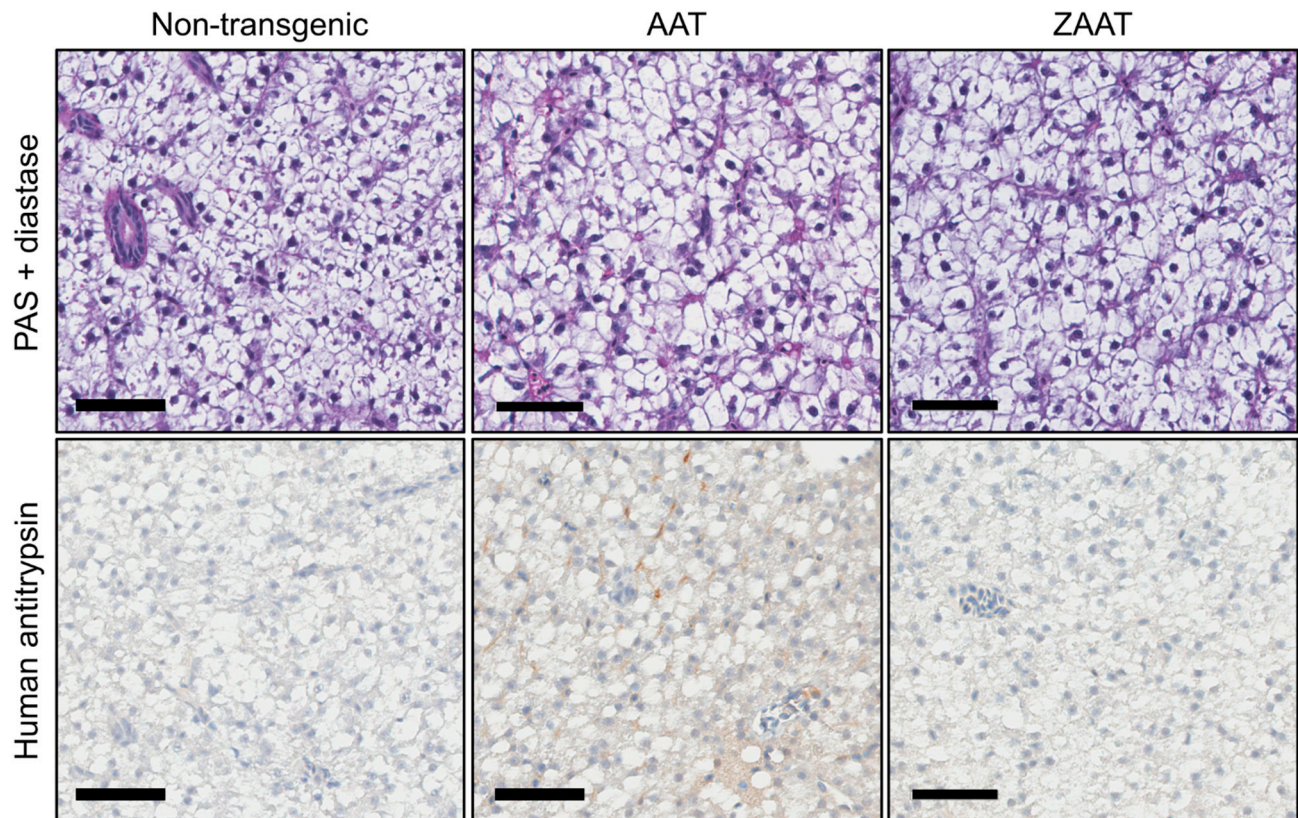


Figure S1. Absence of ZAAT-containing inclusions in transgenic zebrafish liver.

Periodic acid-Schiff (PAS) staining with diastase (top panels) and immunohistochemical staining using a polyclonal guinea pig antibody against human α 1-antitrypsin (bottom panel) was performed on 3 μ m thick paraffin liver sections from non-transgenic (left panels), AAT-transgenic (middle panels) and ZAAT-transgenic (right panels) adult zebrafish. Scale bar represents 50 μ m.

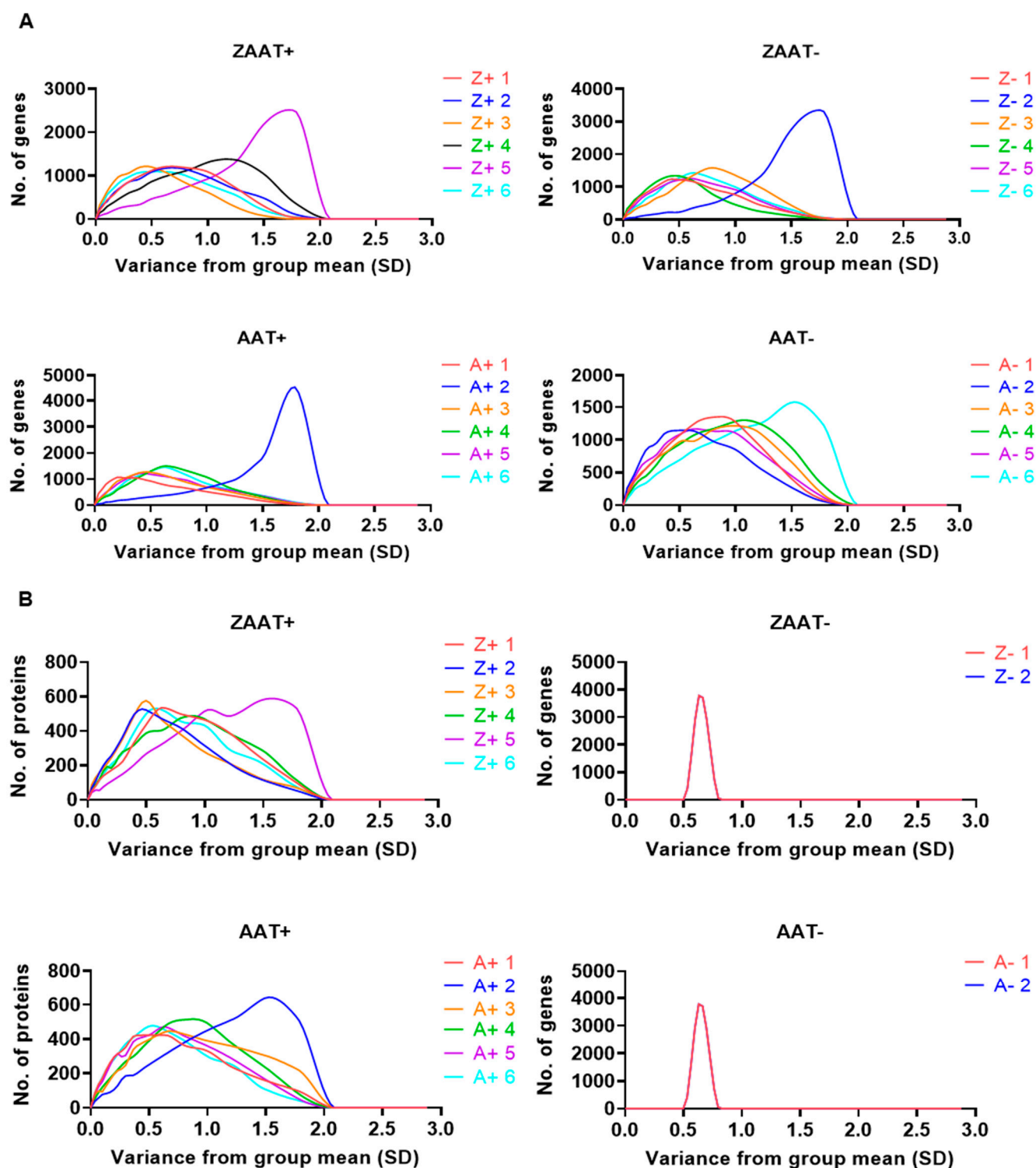


Figure S2. Variation analysis identifies outlier in bioinformatic experiments.

RPKM from RNA-seq and protein counts from LCMS/MS were converted into Z-scores. The number of genes/proteins is plotted against the absolute values of Z-score. Variation analysis of **a)** RNA-seq data identified 1 out of 6 fish in each group (Z+ 5, Z- 2, A+ 2 and A- 6) as outlier, and in **b)** LCMS data, one transgenic fish was identified as outlier in each transgenic group (A+ 2, Z+ 5), consistent RNA-seq. No outlier was identified from non-transgenic sibling groups due to small sample size. These samples were excluded in the downstream differential expression analysis.

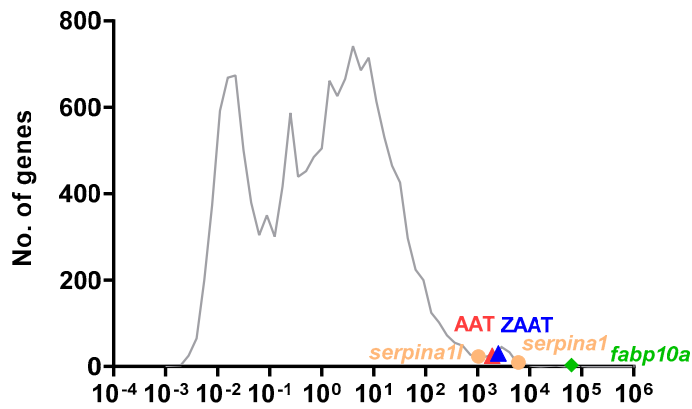


Figure S3. Comparison of transgene expression to endogenous antitrypsin.

Frequency distribution of protein-coding transcripts in zebrafish livers from RNA-seq data, averaging RPKM for each gene from all fish across the four genotype groups. The red triangle indicates the expression of AAT and blue triangle indicates the expression of the ZAAT transgene.

	Proteomics		Transcriptomics	
Student's t-test	Min	Max	Min	Max
Z+ vs. A+	0.000	0.050	0.000	0.010
Z+ vs. [A+Z+]	0.000	0.250	0.000	0.010
Z+ vs. Z-	0.000	0.250	0.000	0.010
Z- vs. A-	0.050	1.000	0.050	1.000
[FDR] threshold	0.250		0.010	
Differential exp genes	77		435	
% of total peptide/genes	1.74%		1.54%	

Figure S4. Statistical parameters used dysregulation expression analysis

Summary of Analysis - Analysis - Data - Human gene filtered 2(1)		
Top Canonical Pathways		
Name	p-value	Overlap
Superpathway of Cholesterol Biosynthesis	2.06E-14	44.4 % 12/27
Cholesterol Biosynthesis I	1.18E-09	53.8 % 7/13
Cholesterol Biosynthesis II (via 24,25-dihydrolanosterol)	1.18E-09	53.8 % 7/13
Cholesterol Biosynthesis III (via Desmosterol)	1.18E-09	53.8 % 7/13
Superpathway of Geranylgeranyldiphosphate Biosynthesis I (via Mevalonate)	8.19E-06	31.2 % 5/16
Top Upstream Regulators		
Upstream Regulator	p-value of overlap	Predicted Activation
SH3TC2	1.16E-12	
SREBF2	7.25E-10	Inhibited
SCAP	1.45E-09	Inhibited
SIRT2	2.83E-08	Inhibited
pitavastatin	6.33E-08	Inhibited

Figure S5. Ingenuity pathway analysis of RNA-seq data.

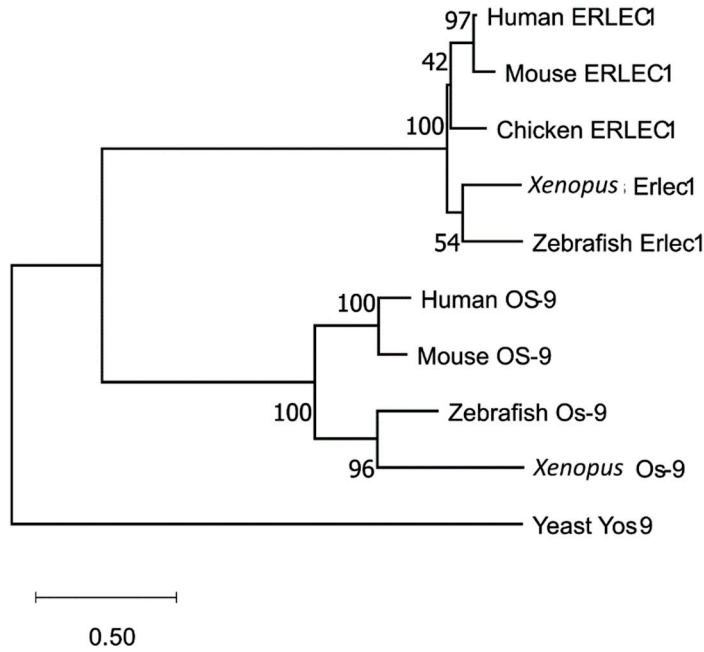


Figure S6. Phylogenetic analysis of ER lectins.

ERLEC1 and OS-9 protein sequences from human, mouse, chicken, *Xenopus*, zebrafish, and yeast were aligned using Clustal-W. Evolutionary history was inferred by using the Maximum Likelihood method and Jones et al. w/freq. model. The tree was calculated from the alignment using Molecular Evolutionary Genetics Analysis software, version 10 (MEGA X). The percentage of trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the Jones-Taylor-Thornton (JTT) model. Scale bar refers to an evolutionary distance (number of substitutions per site) of 0.5.

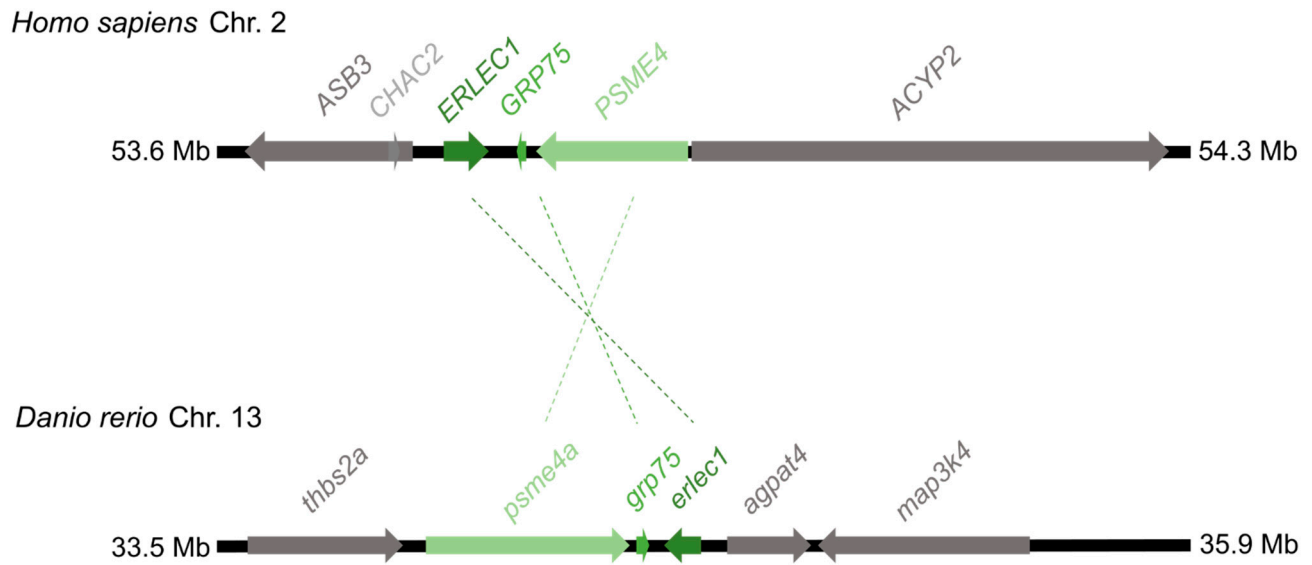


Figure S7. Synteny relationships of *erlec1* gene loci in human and zebrafish.

Mapped genomes of *Homo sapiens* and *Danio rerio* were used to identify conserved gene neighbours of *erlec1*.

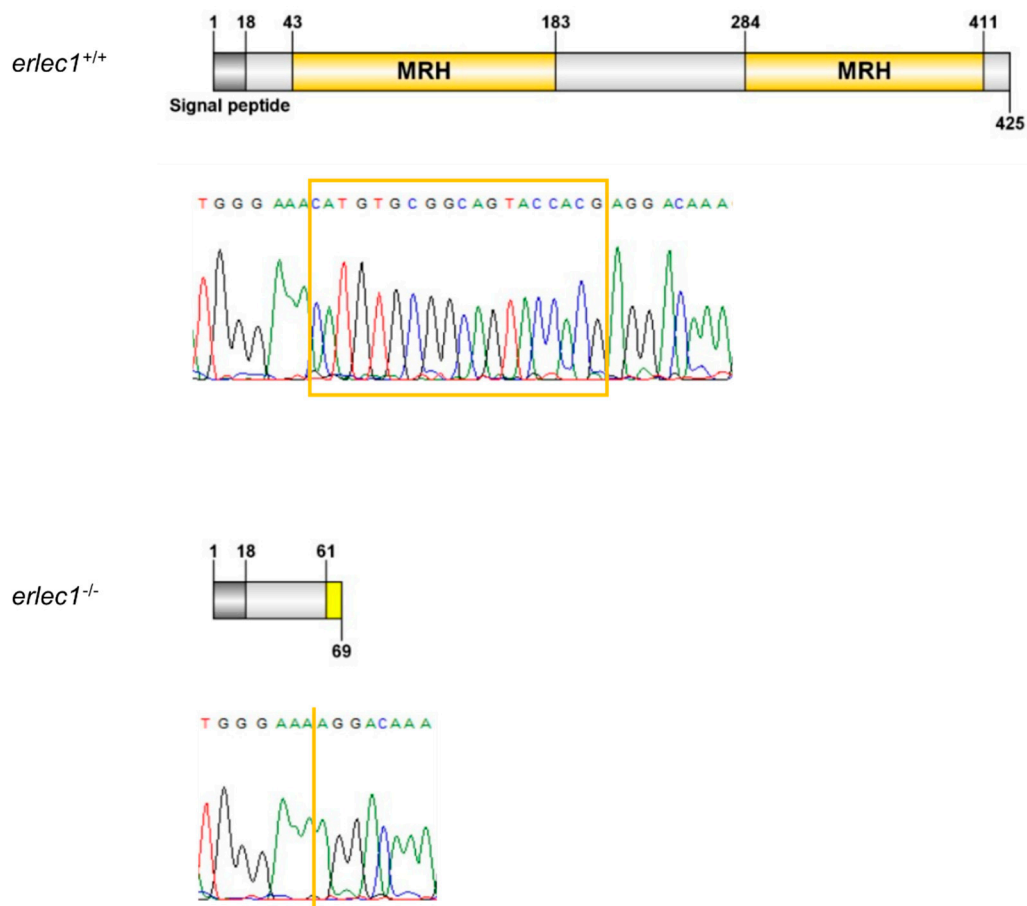


Figure S8. Sequence validation of *erlec1* mutant.

Sequencing of generation F2 homozygotes confirmed a 19 bp deletion at nucleotide positions 184-202 (outlined in yellow), resulting in a frameshift that added 8 amino acids (light yellow) from position 61 before a stop codon. MRH = mannose-6-phosphate receptor homology domain.

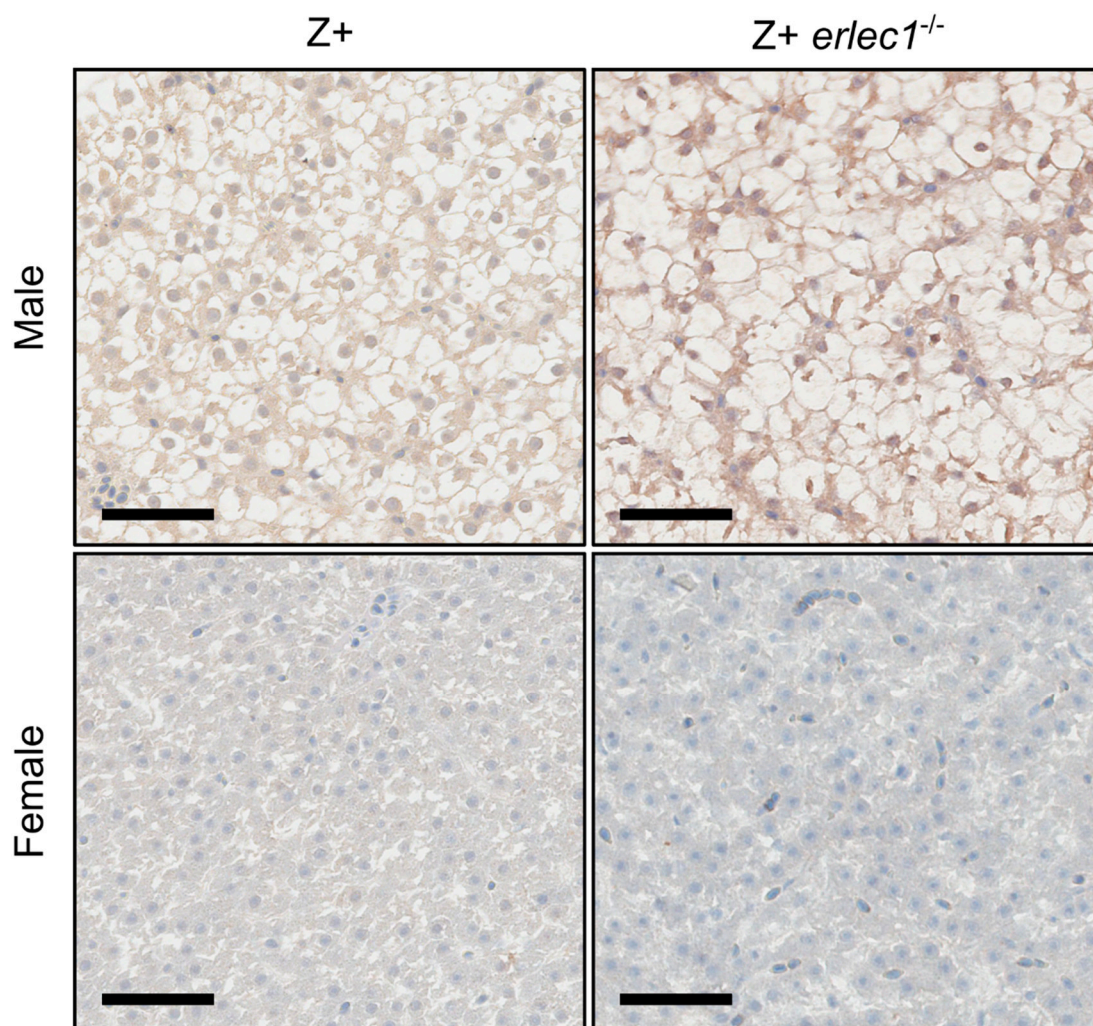
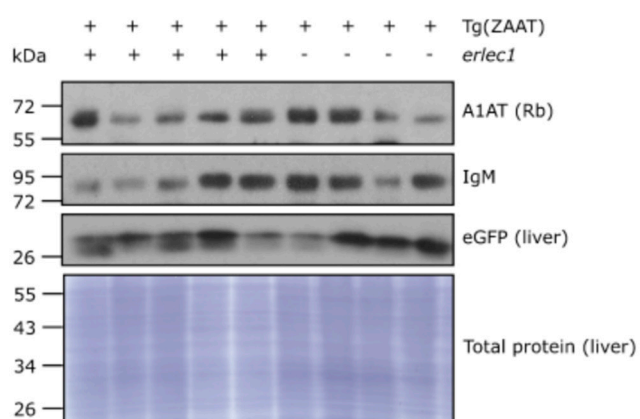


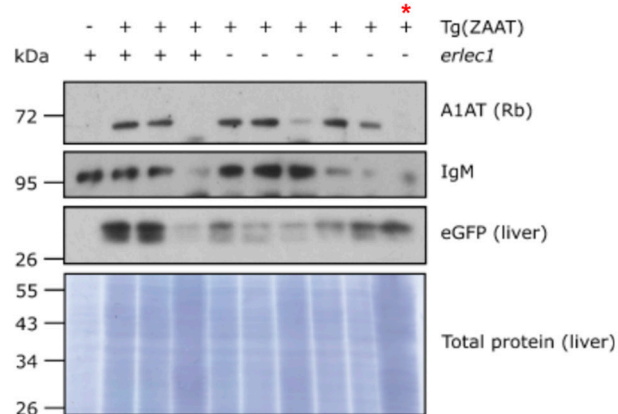
Figure S9. Immunohistochemical staining of *erlec1* mutant expressing ZAAT.

Representative images of 3 μm thick paraffin zebrafish liver sections stained for human antitrypsin. Scale bar represents 50 μm.

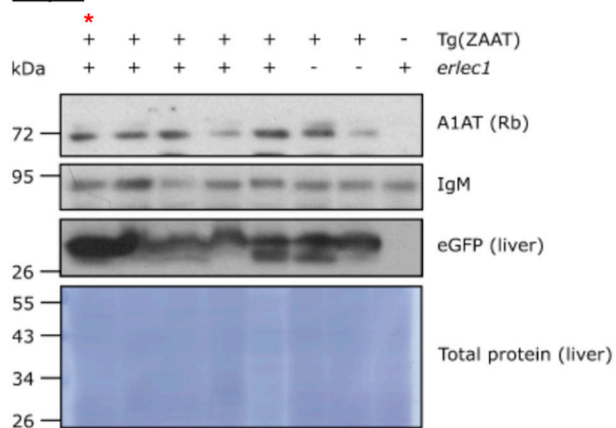
Rep 1



Rep 2



Rep 3



Rep 4

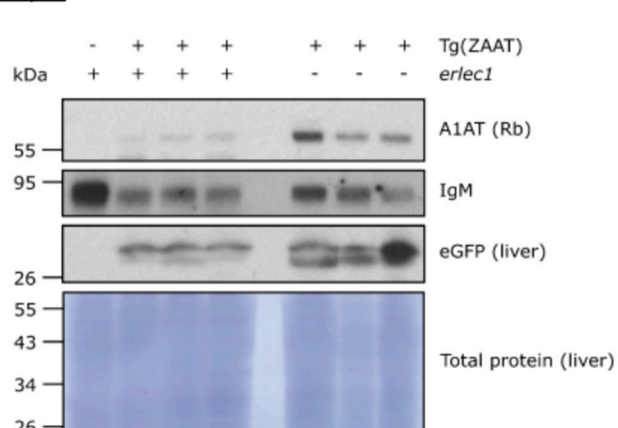


Figure S10. Immunoblots indicating the circulating levels of ZAAT in *erlec1*^{-/-} zebrafish.

Red asterisks indicate outliers determined by the ROUT method (Q=1%), and these data are excluded from the analysis.

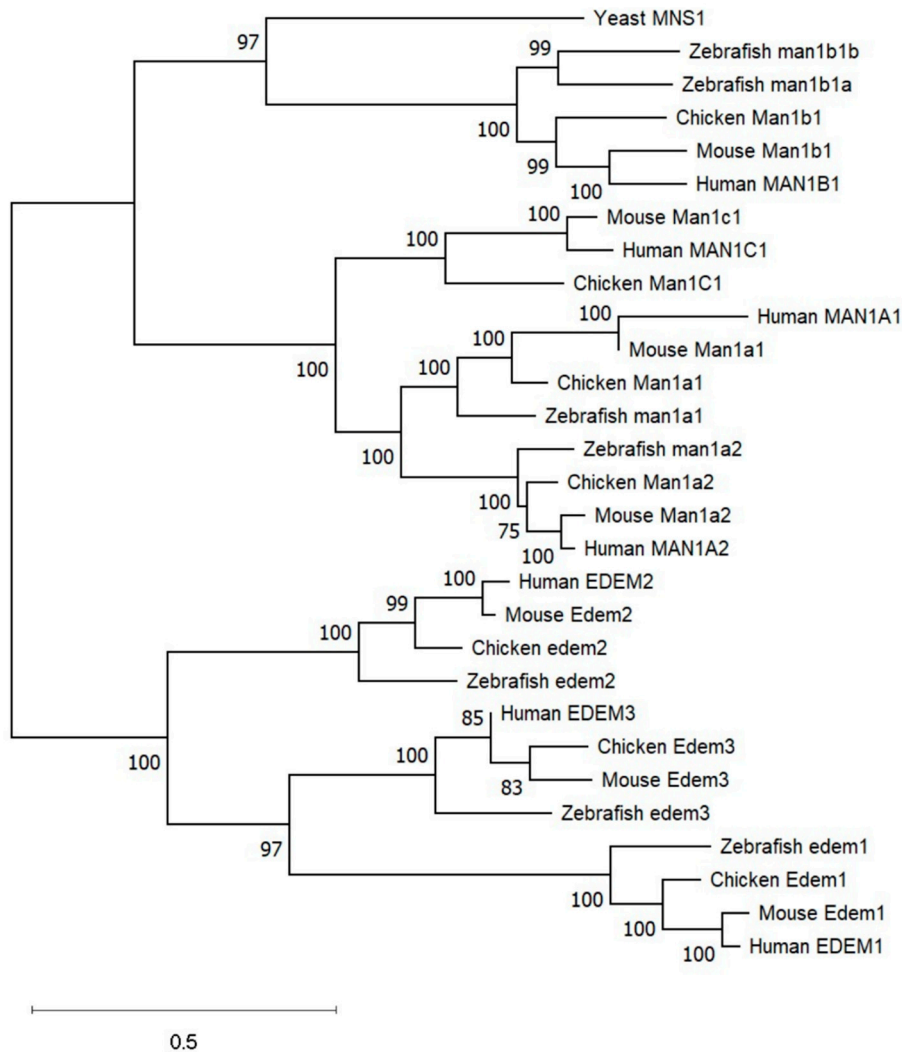


Figure S11. Phylogenetic analysis of glycoside hydrolase family 47 proteins.

Glycoside hydrolase family 47 (GH47) protein sequences from human, mouse, chicken, zebrafish, and yeast were aligned using Clustal-W. Evolutionary history was inferred by using the Maximum Likelihood method and Jones *et al.* w/freq. model. The tree was calculated from the alignment using Molecular Evolutionary Genetics Analysis software, version 10 (MEGA X). The percentage of trees in which the associated taxa clustered together in the bootstrap test (1000 replicates) are shown next to the branches. Initial tree(s) for the heuristic search were obtained automatically by applying Neighbor-Join and BioNJ algorithms to a matrix of pairwise distances estimated using the Jones-Taylor-Thornton (JTT) model. Scale bar refers to an evolutionary distance (number of substitutions per site) of 0.5.

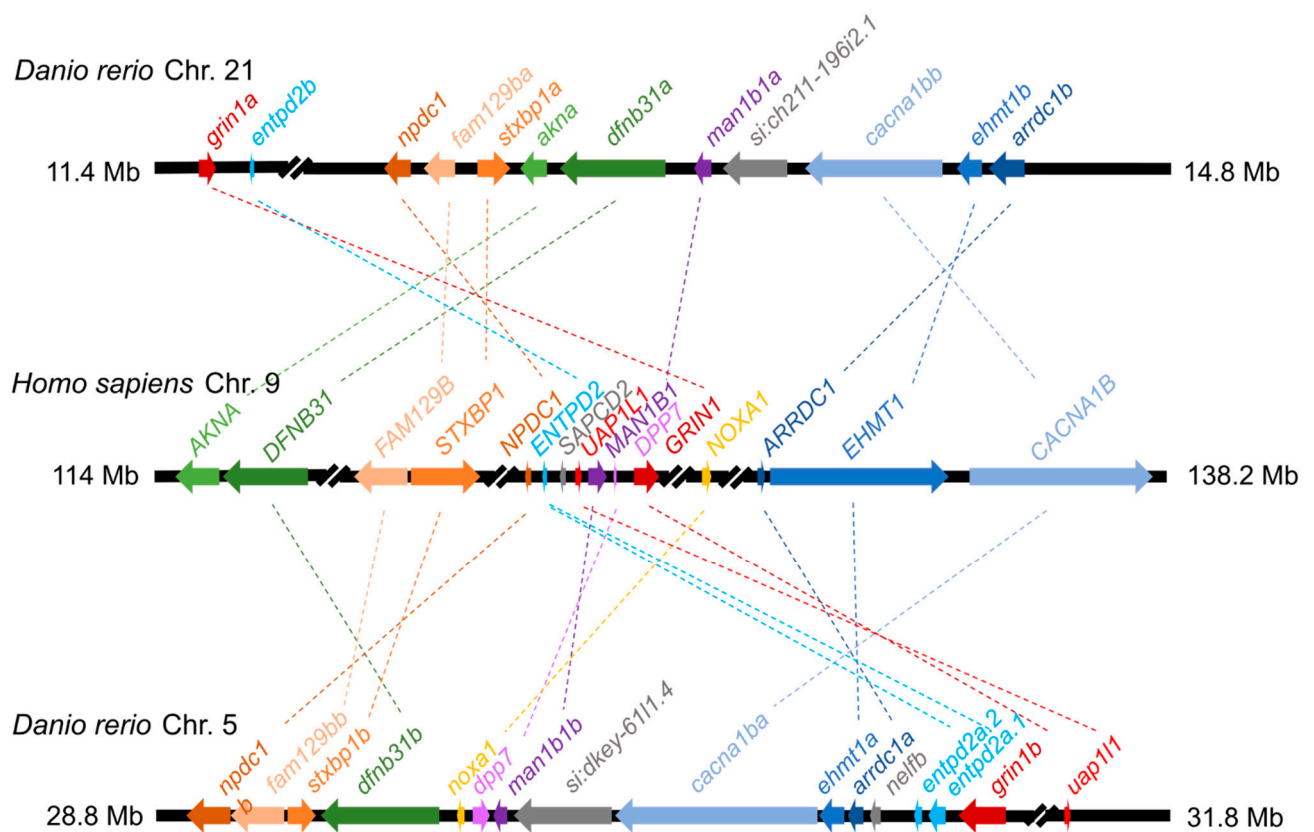


Figure S12. Synteny relationships of *man1b1* gene loci in human and zebrafish.

Mapped genomes of *Homo sapiens* and *Danio rerio* were used to identify conserved gene neighbours of *man1b1a* and *man1b1b*.

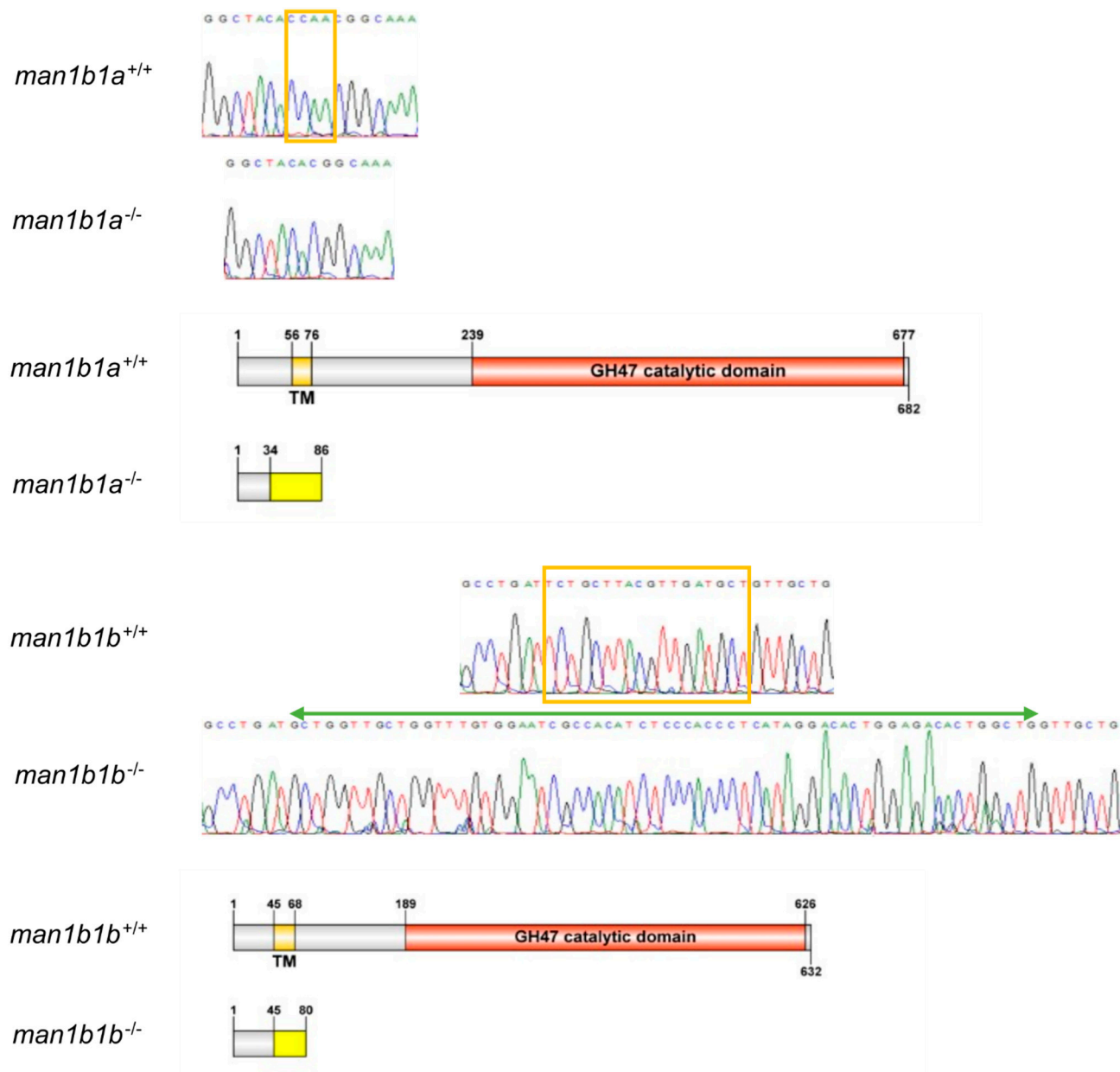


Figure S13. Sequence validation of *man1b1a* and *man1b1b* mutants.

Sequencing of F2 homozygotes confirms a 4 bp deletion at positions 101-104 for *man1b1a*, resulting in frameshift leading to insertion of 52 amino acids (yellow) at position 34 followed by a premature stop codon. Sequencing of *man1b1b* screening PCR product confirms an 18 bp deletion (outlined in yellow) with 65 bp insertion (indicated by green arrow), resulting in a net insertion of 47 bp and a frameshift leading to insertion of 35 amino acids (yellow) at position 45 followed by a premature stop codon. TM = transmembrane domain.

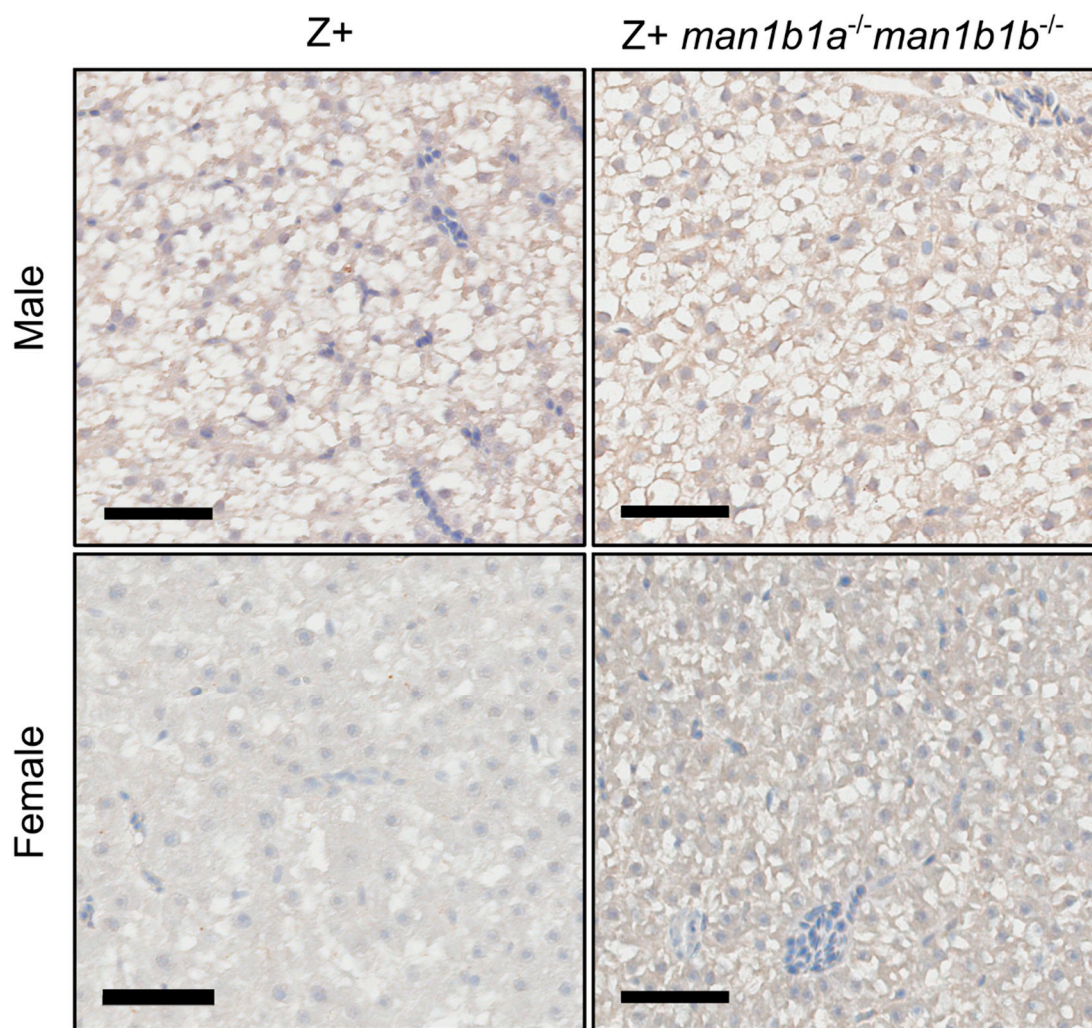
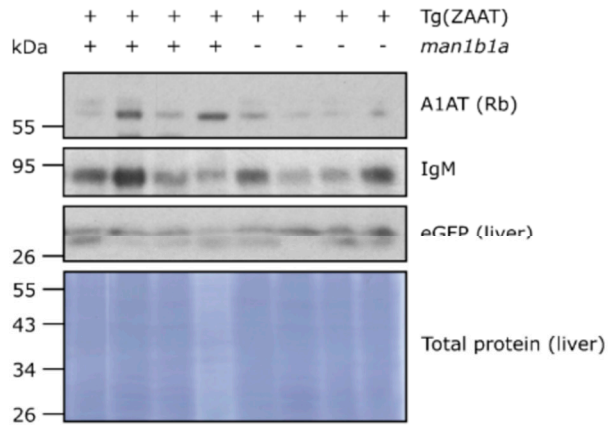


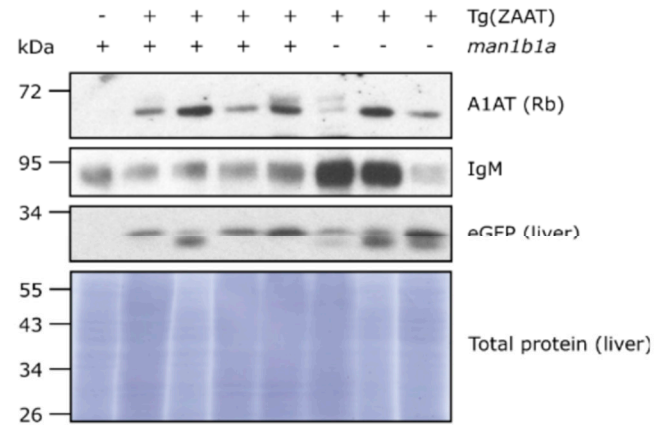
Figure S14. Immunohistochemical staining of *man1b1* double mutant expressing ZAAT.

Representative images of 3 μ m thick paraffin zebrafish liver sections stained for human antitrypsin. Scale bar represents 50 μ m.

Rep 1



Rep 2



Rep 3

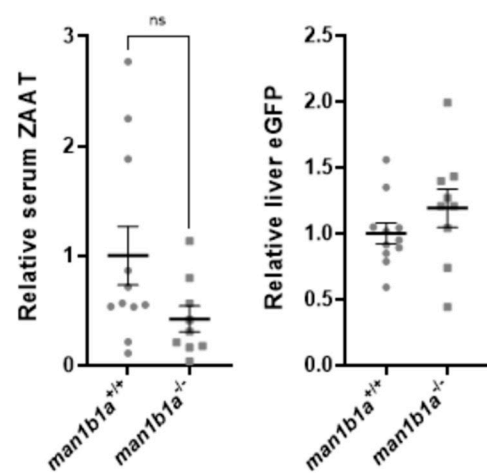
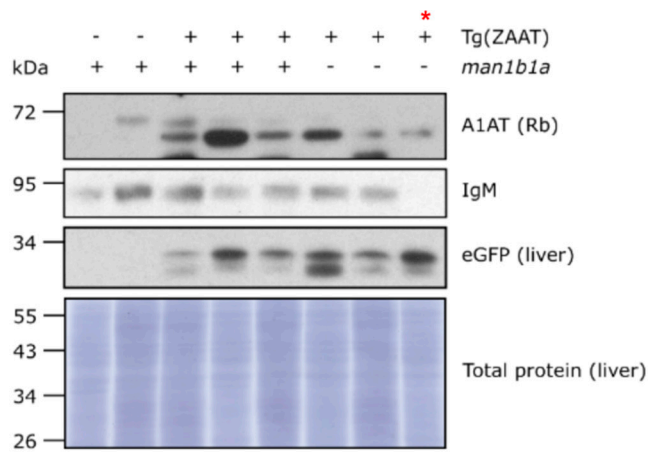


Figure S15. Immunoblots indicating the circulating levels of ZAAT in *man1b1a*^{-/-} zebrafish.

Red asterisks indicate outliers determined by the ROUT method (Q=1%), and these data are excluded from the analysis. Bottom right panel shows quantitation of protein signal by densitometry pooled from three independent experiments, with each point representing an individual fish. Statistical significance was determined by Unpaired Student's t-test. ns = non-significant.

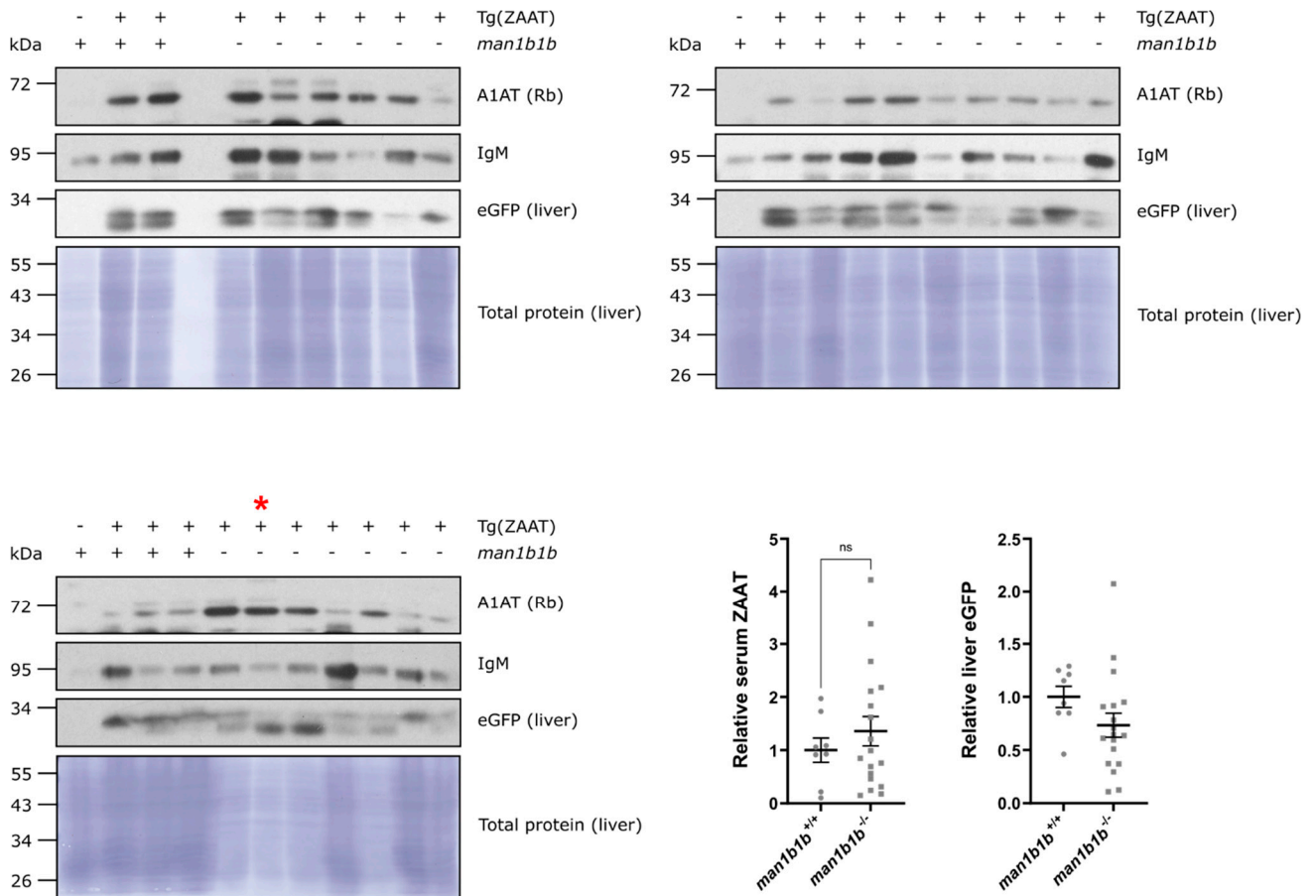


Figure S16. Immunoblots indicating the circulating levels of ZAAT in *man1b1b*^{-/-} zebrafish

Red asterisks indicate outliers determined by the ROUT method (Q=1%), and these data are excluded from the analysis. Bottom right panel shows quantitation of protein signal by densitometry pooled from three independent experiments, with each point representing an individual fish. Statistical significance was determined by Unpaired Student's t-test. ns = non-significant.

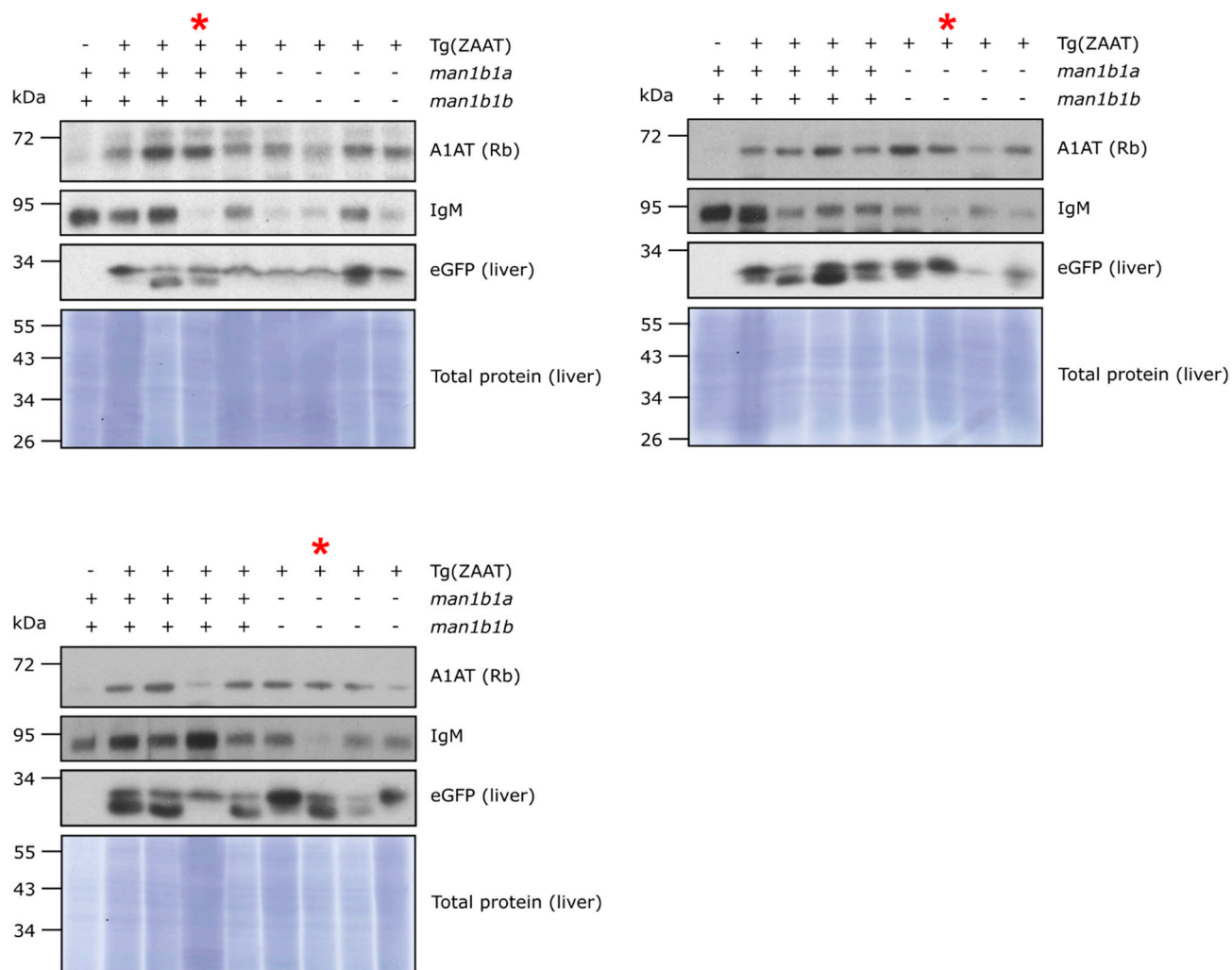


Figure S17. Immunoblots indicating the circulating levels of ZAAT in *man1b1a*^{-/-} *man1b1b*^{-/-} zebrafish.

Red asterisks indicate outliers determined by the ROUT method (Q=1%), and these data are excluded from the analysis.

Table S1. List of DEGs identified from RNA-seq

Gene	Product	Z+/A+	A+/A-	Z+/Z-
<i>klhl24b</i>	kelch-like family member 24b	16.89	0.86	12.13
<i>frmd4bb</i>	FERM domain containing 4Bb	16.35	0.56	8.00
<i>bco2l</i>	beta-carotene 15, 15-dioxygenase 2, like	8.13	1.72	5.86
<i>fam222a</i>	family with sequence similarity 222, member A	6.24	0.60	4.89
<i>ulk2</i>	unc-51 like autophagy activating kinase 2	6.17	1.25	6.45
<i>lmbr1l</i>	limb development membrane protein 1-like	6.16	0.53	2.23
<i>fbxo25</i>	F-box protein 25	6.05	1.77	9.06
<i>si:ch211-232d10.1</i>	si:ch211-232d10.1	5.73	0.91	3.36
<i>exo5</i>	exonuclease 5	5.4	1.00	5.10
<i>ulk1a</i>	unc-51 like autophagy activating kinase 1a	5.27	0.95	5.90
<i>cyhr1</i>	cysteine/histidine-rich 1	5.23	0.51	2.68
<i>tle3b</i>	transducin-like enhancer of split 3b	5.13	1.05	8.28
<i>mtx3</i>	metaxin 3	5.11	1.32	4.76
<i>trim44</i>	tripartite motif containing 44	4.95	0.85	3.46
<i>si:ch73-386h18.1</i>	si:ch73-386h18.1	4.95	0.80	4.20
<i>irs2a</i>	insulin receptor substrate 2a	4.84	0.86	3.51
<i>klhl32</i>	kelch-like family member 32	4.52	1.55	4.82
<i>crbn</i>	cereblon	4.37	1.02	3.23
<i>stk11ip</i>	serine/threonine kinase 11 interacting protein	4.34	0.68	5.66
<i>pel12</i>	pellino E3 ubiquitin protein ligase family member 2	4.21	0.66	3.68
<i>slc34a2b</i>	solute carrier family 34 (type II sodium/phosphate cotransporter), member 2b	4.14	0.84	3.58
<i>abo</i>	ABO blood group (transferase A, alpha 1-3-N-acetylgalactosaminyltransferase; transferase B, alpha 1-3-galactosyltransferase)	4.08	1.68	6.87
<i>tesk2</i>	testis-specific kinase 2	4.08	0.61	3.29
<i>invs</i>	inversin	4.04	0.95	2.69
<i>fir67</i>	finTRIM family, member 67	4.02	0.89	3.41
<i>nav2b</i>	neuron navigator 2b	3.99	1.09	4.38
<i>sik2a</i>	salt-inducible kinase 2a	3.96	1.75	6.32
<i>tbc1a</i>	tubulin folding cofactor E-like a	3.95	1.10	4.03
<i>rapgef3</i>	Rap guanine nucleotide exchange factor (GEF) 3	3.9	0.49	3.12
<i>cyp2r1</i>	cytochrome P450, family 2, subfamily R, polypeptide 1	3.83	1.11	4.23
<i>nr2c2</i>	nuclear receptor subfamily 2, group C, member 2	3.66	0.76	2.87
<i>cyl1da</i>	cylindromatosis (turban tumor syndrome), a	3.65	0.66	1.97
<i>nocta</i>	nocturnin a	3.62	0.95	2.46
<i>hfe2</i>	hemochromatosis type 2	3.59	0.74	3.56
<i>lmbrd2b</i>	LMBR1 domain containing 2b	3.56	0.69	2.17
<i>ankib1b</i>	ankyrin repeat and IBR domain containing 1b	3.52	0.94	3.51
<i>rmdn2</i>	regulator of microtubule dynamics 2	3.5	1.70	5.10
<i>katnal1</i>	katanin p60 subunit A-like 1	3.49	0.90	2.33
<i>mtmr3</i>	myotubularin related protein 3	3.49	1.21	3.84
<i>evi5b</i>	ecotropic viral integration site 5b	3.47	0.90	4.26
<i>dcun1d4</i>	DCN1, defective in cullin neddylation 1, domain containing 4 (S. cerevisiae)	3.44	1.01	4.44
<i>tada2a</i>	transcriptional adaptor 2A	3.34	0.91	2.89

<i>bnip4</i>	BCL2 interacting protein 4	3.33	0.79	2.41
<i>pomk</i>	protein-O-mannose kinase	3.29	0.88	2.79
<i>wu:fb44b02</i>	wu:fb44b02	3.23	1.21	2.99
<i>wdr26a</i>	WD repeat domain 26a	3.21	0.80	2.66
<i>ssfa2</i>	sperm specific antigen 2	3.12	0.73	1.80
<i>kifap3a</i>	kinesin-associated protein 3a	3.08	0.87	2.00
<i>syne3</i>	spectrin repeat containing, nuclear envelope family member 3	3.07	1.27	3.76
<i>FO834800.1</i>		3.01	0.50	2.01
<i>wdr24</i>	WD repeat domain 24	3	1.31	3.73
<i>fam222ba</i>	family with sequence similarity 222, member Ba	2.97	0.96	3.84
<i>si:dkey-38p12.3</i>	si:dkey-38p12.3	2.95	0.90	2.77
<i>map3k4</i>	mitogen-activated protein kinase kinase kinase 4	2.94	1.05	3.05
<i>creb3l2</i>	cAMP responsive element binding protein 3-like 2	2.93	0.90	3.14
<i>rufy2</i>	RUN and FYVE domain containing 2	2.91	1.11	2.57
<i>si:dkey-40c23.1</i>	si:dkey-40c23.1	2.91	1.44	2.99
<i>rassf3</i>	Ras association (RalGDS/AF-6) domain family member 3	2.9	1.24	2.10
<i>agtpbp1</i>	ATP/GTP binding protein 1	2.88	0.77	1.88
<i>mtmr11</i>	myotubularin related protein 11	2.81	1.56	4.06
<i>nr3c1</i>	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	2.8	0.88	2.50
<i>fam160b2</i>	family with sequence similarity 160, member B2	2.79	1.01	2.73
<i>cpeb3</i>	cytoplasmic polyadenylation element binding protein 3	2.72	0.18	0.38
<i>si:dkey-246g23.4</i>	si:dkey-246g23.4	2.71	1.97	6.82
<i>coq8a</i>	coenzyme Q8A	2.71	0.87	2.25
<i>scube2</i>	signal peptide, CUB domain, EGF-like 2	2.7	1.22	2.73
<i>ulk1b</i>	unc-51 like autophagy activating kinase 1	2.69	1.56	3.86
<i>si:dkey-249d8.1</i>	si:dkey-249d8.1	2.69	0.88	1.97
<i>stard3</i>	StAR-related lipid transfer (START) domain containing 3	2.68	0.63	1.78
<i>arhgef16</i>	Rho guanine nucleotide exchange factor (GEF) 16	2.68	1.51	2.79
<i>rab11bb</i>	RAB11B, member RAS oncogene family, b	2.67	0.81	1.84
<i>hdac6</i>	histone deacetylase 6	2.67	0.85	1.97
<i>stag2a</i>	stromal antigen 2a	2.67	0.81	2.00
<i>si:ch211-235o23.1</i>	si:ch211-235o23.1	2.65	0.79	2.01
<i>nlrc5</i>	NLR family, CARD domain containing 5	2.65	0.90	2.46
<i>fncl3a</i>	fibronectin type III domain containing 3A	2.64	0.76	2.27
<i>si:dkey-29p10.4</i>	si:dkey-29p10.4	2.61	0.71	1.91
<i>brip1</i>	BRCA1 interacting protein C-terminal helicase 1	2.61	1.40	2.89
<i>zfyve26</i>	zinc finger, FYVE domain containing 26	2.59	0.80	2.31
<i>gfod2</i>	glucose-fructose oxidoreductase domain containing 2	2.58	1.03	3.25
<i>lrrc45</i>	leucine rich repeat containing 45	2.58	1.24	3.20
<i>zbtb41</i>	zinc finger and BTB domain containing 41	2.58	1.25	3.01
<i>vrk2</i>	vaccinia related kinase 2	2.57	0.84	1.78
<i>irgf1</i>	immunity-related GTPase family, f1	2.56	0.80	1.87
<i>zgc:100832</i>	zgc:100832	2.54	0.95	2.22
<i>inpp4aa</i>	inositol polyphosphate-4-phosphatase type I Aa	2.54	1.49	3.41
<i>si:dkey-205i10.1</i>	si:dkey-205i10.1	2.54	1.63	4.08
<i>ghdc</i>	GH3 domain containing	2.53	0.88	1.87
<i>kif7</i>	kinesin family member 7	2.52	1.24	2.64

<i>irf2</i>	interferon regulatory factor 2	2.52	0.95	2.55
<i>senp7b</i>	SUMO1/sentrin specific peptidase 7b	2.51	1.26	3.63
<i>si:ch211-85n16.4</i>	si:ch211-85n16.4	2.5	0.92	2.58
<i>met</i>	MET proto-oncogene, receptor tyrosine kinase	2.49	0.82	3.12
<i>nfkbie</i>	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, epsilon	2.49	1.03	3.66
<i>zranb1b</i>	zinc finger, RAN-binding domain containing 1b	2.47	1.20	3.12
<i>flcn</i>	folliculin	2.47	0.79	1.71
<i>unkl</i>	unkempt family zinc finger-like	2.47	0.92	1.89
<i>si:ch211-216l23.2</i>	si:ch211-216l23.2	2.47	0.95	2.22
<i>herc3</i>	HECT and RLD domain containing E3 ubiquitin protein ligase 3	2.47	1.16	2.36
<i>zdhhc9</i>	zinc finger, DHHC-type containing 9	2.46	0.96	2.39
<i>trmt44</i>	tRNA methyltransferase 44 homolog	2.46	0.84	2.03
<i>mertka</i>	c-mer proto-oncogene tyrosine kinase a	2.45	1.13	2.89
<i>kcng4b</i>	potassium voltage-gated channel, subfamily G, member 4b	2.44	4.31	23.59
<i>wdtc1</i>	WD and tetratricopeptide repeats 1	2.43	0.69	1.67
<i>uacaa</i>	uveal autoantigen with coiled-coil domains and ankyrin repeats a	2.43	1.61	3.10
<i>tfpt</i>	TCF3 (E2A) fusion partner	2.43	1.07	1.96
<i>efcab7</i>	EF-hand calcium binding domain 7	2.43	1.48	3.43
<i>notch3</i>	notch 3	2.42	1.16	2.22
<i>si:dkey-24l11.2</i>	si:dkey-24l11.2	2.41	0.85	1.92
<i>zgc:153151</i>	zgc:153151	2.41	0.90	2.17
<i>bckdk</i>	branched chain ketoacid dehydrogenase kinase	2.4	0.67	1.97
<i>marveld2a</i>	MARVEL domain containing 2a	2.4	1.01	2.27
<i>als2b</i>	amyotrophic lateral sclerosis 2b (juvenile)	2.4	1.60	2.62
<i>nelfcd</i>	negative elongation factor complex member C/D	2.4	0.96	1.91
<i>abcd4</i>	ATP-binding cassette, sub-family D (ALD), member 4	2.39	0.98	1.99
<i>pxna</i>	paxillin a	2.37	1.65	2.97
<i>ddx59</i>	DEAD (Asp-Glu-Ala-Asp) box polypeptide 59	2.37	1.10	2.46
<i>fbxo3</i>	F-box protein 3	2.37	1.08	2.64
<i>si:dkey-240n22.3</i>	si:dkey-240n22.3	2.36	1.98	3.46
<i>creb3l3l</i>	cAMP responsive element binding protein 3-like 3 like	2.35	0.71	1.62
<i>fbxl6</i>	F-box and leucine-rich repeat protein 6	2.35	1.36	3.61
<i>arhgap27</i>	Rho GTPase activating protein 27	2.33	1.36	2.23
<i>man2c1</i>	mannosidase, alpha, class 2C, member 1	2.33	0.83	1.72
<i>si:ch73-138n13.1</i>	si:ch73-138n13.1	2.33	1.14	2.85
<i>CU207301.3</i>		2.33	1.07	1.91
<i>krit1</i>	KRIT1, ankyrin repeat containing	2.32	1.33	2.51
<i>CLIP4</i>	si:dkeyp-47f9.4	2.31	1.31	2.53
<i>CU856539.2</i>		2.29	1.22	2.16
<i>spast</i>	spastin	2.28	1.22	3.53
<i>smc6</i>	structural maintenance of chromosomes 6	2.27	1.11	2.60
<i>si:ch73-95l15.5</i>	si:ch73-95l15.5	2.27	0.73	1.79
<i>dger6</i>	DiGeorge syndrome critical region gene 6	2.26	0.90	1.99
<i>tspear</i>	thrombospondin-type laminin G domain and EAR repeats a	2.26	1.92	4.69
<i>tnrc6c1</i>	trinucleotide repeat containing 6C1	2.26	1.02	3.43
<i>mfsd4b</i>	major facilitator superfamily domain containing 4B	2.25	0.85	1.93
<i>wdsub1</i>	WD repeat, sterile alpha motif and U-box domain containing 1	2.25	0.82	1.84

<i>recql5</i>	RecQ helicase-like 5	2.25	0.92	1.67
<i>ehmt1a</i>	euchromatic histone-lysine N-methyltransferase 1a	2.25	1.13	2.50
<i>si:dkey-72117.5</i>	si:dkey-72117.5	2.24	1.51	2.06
<i>tmem131l</i>	transmembrane 131 like	2.24	0.99	1.89
<i>zgc:158366</i>	zgc:158366	2.23	0.74	1.55
<i>sirt6</i>	sirtuin 6	2.22	1.05	2.33
<i>ncoa3</i>	nuclear receptor coactivator 3	2.21	0.88	2.03
<i>kdm4b</i>	lysine (K)-specific demethylase 4B	2.2	0.80	1.93
<i>zgc:173581</i>	zgc:173581	2.19	1.01	2.00
<i>rfx1b</i>	regulatory factor X, 1b (influences HLA class II expression)	2.19	1.13	2.17
<i>BX005416.1</i>		2.19	1.08	2.73
<i>slain2</i>	SLAIN motif family, member 2	2.19	1.50	2.81
<i>phf2</i>	PHD finger protein 2	2.19	1.18	2.00
<i>kif3a</i>	kinesin family member 3A	2.18	1.13	2.25
<i>arhgef1b</i>	Rho guanine nucleotide exchange factor (GEF) 1b	2.18	0.91	1.51
<i>pcdh12</i>	protocadherin 12	2.18	1.47	3.63
<i>CABZ01021435.1</i>		2.18	1.32	2.89
<i>capn7</i>	calpain 7	2.18	0.75	1.71
<i>sumf1</i>	sulfatase modifying factor 1	2.17	0.93	1.61
<i>si:dkey-159n16.2</i>	si:dkey-159n16.2	2.17	2.01	3.20
<i>arhgap27l</i>	Rho GTPase activating protein 27, like	2.16	1.35	3.58
<i>ep300b</i>	E1A binding protein p300 b	2.16	1.34	3.34
<i>ap4e1</i>	adaptor-related protein complex 4, epsilon 1 subunit	2.16	0.99	2.04
<i>zgc:123105</i>	zgc:123105	2.16	0.90	1.42
<i>ncoa1</i>	nuclear receptor coactivator 1	2.16	1.40	3.07
<i>calcocola</i>	calcium binding and coiled-coil domain 1a	2.15	1.28	3.16
<i>rabgap1</i>	RAB GTPase activating protein 1	2.15	1.63	2.66
<i>nav2a</i>	neuron navigator 2a	2.14	1.62	6.96
<i>dbpa</i>	D site albumin promoter binding protein a	2.14	0.95	2.11
<i>ift172</i>	intraflagellar transport 172	2.14	1.19	2.04
<i>si:dkey-165a24.9</i>	si:dkey-165a24.9	2.14	1.38	2.48
<i>ptpn2a</i>	protein tyrosine phosphatase, non-receptor type 2, a	2.13	0.78	1.77
<i>CR388364.2</i>		2.13	2.13	4.82
<i>nt5dc2</i>	5'-nucleotidase domain containing 2	2.13	0.77	1.57
<i>tead1a</i>	TEA domain family member 1a	2.12	1.44	3.53
<i>trpm6</i>	transient receptor potential cation channel, subfamily M, member 6	2.12	1.74	2.45
<i>pld1a</i>	phospholipase D1a	2.12	0.74	1.79
<i>trpm2</i>	transient receptor potential cation channel, subfamily M, member 2	2.12	1.91	3.27
<i>si:dkey-240n22.6</i>	si:dkey-240n22.6	2.12	1.00	2.04
<i>rnf20</i>	ring finger protein 20, E3 ubiquitin protein ligase	2.12	1.00	2.11
<i>cetn4</i>	centrin 4	2.11	0.92	1.80
<i>tmem120a</i>	transmembrane protein 120A	2.11	1.16	2.19
<i>mgea5</i>	meningioma expressed antigen 5 (hyaluronidase)	2.1	0.97	2.73
<i>brdt</i>	bromodomain, testis-specific	2.1	1.85	3.05
<i>usp2a</i>	ubiquitin specific peptidase 2a	2.1	1.17	2.60
<i>mtmr8</i>	myotubularin related protein 8	2.09	1.36	2.33
<i>sh3gl3a</i>	SH3-domain GRB2-like 3a	2.08	0.97	3.71
<i>qser1</i>	glutamine and serine rich 1	2.08	1.14	2.41

<i>clk4a</i>	CDC-like kinase 4a	2.07	1.78	3.07
<i>CR759794.1</i>		2.07	1.17	2.58
<i>als2a</i>	amyotrophic lateral sclerosis 2a (juvenile)	2.07	1.28	2.03
<i>lims1</i>	LIM and senescent cell antigen-like domains 1	2.06	0.87	2.04
<i>rb1cc1</i>	RB1-inducible coiled-coil 1	2.03	0.67	1.45
<i>ppp2r3c</i>	protein phosphatase 2, regulatory subunit B", gamma	2.03	0.86	1.47
<i>gpatch11</i>	G patch domain containing 11	2.03	0.74	1.41
<i>kdm4c</i>	lysine (K)-specific demethylase 4C	2.03	0.98	1.83
<i>smchd1</i>	structural maintenance of chromosomes flexible hinge domain containing 1	2.02	0.78	1.56
<i>epg5</i>	ectopic P-granules autophagy protein 5 homolog (C. elegans)	2.01	1.30	2.31
<i>chd11</i>	chromodomain helicase DNA binding protein 1-like	2	1.15	1.96
<i>prkag2b</i>	protein kinase, AMP-activated, gamma 2 non-catalytic subunit b	1.99	0.82	2.03
<i>tjp2a</i>	tight junction protein 2a (zona occludens 2)	1.98	0.90	1.99
<i>chfr</i>	checkpoint with forkhead and ring finger domains, E3 ubiquitin protein ligase	1.97	0.93	1.58
<i>appl1</i>	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 1	1.97	0.84	1.88
<i>nhs11b</i>	NHS-like 1b	1.97	1.48	2.73
<i>zgc:153012</i>	zgc:153012	1.96	0.88	2.04
<i>si:dkey-262g12.14</i>	si:dkey-262g12.14	1.95	1.40	2.35
<i>actb2</i>	actin, beta 2	1.95	0.83	1.64
<i>nr1h3</i>	nuclear receptor subfamily 1, group H, member 3	1.94	0.78	1.71
<i>kmt2e</i>	lysine (K)-specific methyltransferase 2E	1.94	1.24	2.57
<i>zgc:152774</i>	zgc:152774	1.93	1.03	1.87
<i>shc2</i>	SHC (Src homology 2 domain containing) transforming protein 2	1.93	1.07	2.45
<i>def6c</i>	differentially expressed in FDCP 6c homolog	1.92	0.85	2.38
<i>mkrn1</i>	makorin, ring finger protein, 1	1.92	1.20	2.71
<i>pak2a</i>	p21 protein (Cdc42/Rac)-activated kinase 2a	1.92	0.88	1.66
<i>taf3</i>	TAF3 RNA polymerase II, TATA box binding protein (TBP)-associated facto	1.92	0.88	1.78
<i>raf1a</i>	Raf-1 proto-oncogene, serine/threonine kinase a	1.91	1.04	1.82
<i>selenoo1</i>	selenoprotein O1	1.91	1.05	1.96
<i>lnx2b</i>	ligand of numb-protein X 2b	1.89	1.37	2.08
<i>mcf2la</i>	mcf.2 cell line derived transforming sequence-like a	1.89	0.96	1.68
<i>cyl1d1</i>	cylindromatosis (turban tumor syndrome), like	1.89	0.78	1.46
<i>ptpn13</i>	protein tyrosine phosphatase, non-receptor type 13	1.89	1.38	2.46
<i>rbm18</i>	RNA binding motif protein 18	1.89	0.88	1.84
<i>alkbh3</i>	alkB homolog 3, alpha-ketoglutarate-dependent dioxygenase	1.88	1.42	2.60
<i>gnpnat1</i>	glucosamine-phosphate N-acetyltransferase 1	1.88	1.15	2.79
<i>ldb2a</i>	LIM domain binding 2a	1.88	1.10	1.99
<i>CZQB01141835.2</i>		1.88	1.10	2.33
<i>rab40b</i>	RAB40B, member RAS oncogene family	1.87	0.79	1.77
<i>dffb</i>	DNA fragmentation factor, beta polypeptide (caspase-activated DNase)	1.87	0.97	1.99
<i>dyrk1b</i>	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 1B	1.87	1.05	2.36
<i>per2</i>	period circadian clock 2	1.85	1.09	2.30
<i>gtf2a11</i>	general transcription factor IIA, 1-like	1.85	1.02	1.73
<i>SLC35G1</i>	si:ch211-197g18.2	1.85	1.04	1.79
<i>wdr33</i>	WD repeat domain 33	1.84	1.19	2.06
<i>si:ch211-261p9.4</i>	si:ch211-261p9.4	1.84	0.84	1.53
<i>pkp3b</i>	plakophilin 3b	1.84	0.90	1.85

<i>usp48</i>	ubiquitin specific peptidase 48	1.84	1.03	1.78
<i>znf384l</i>	zinc finger protein 384 like	1.84	1.24	2.20
<i>fpgs</i>	folylpolyglutamate synthase	1.84	1.06	1.56
<i>ift52</i>	intraflagellar transport 52 homolog (Chlamydomonas)	1.83	1.10	1.88
<i>ormdl1</i>	ORMDL sphingolipid biosynthesis regulator 1	1.83	1.17	2.31
<i>arhgef11</i>	Rho guanine nucleotide exchange factor (GEF) 11	1.83	1.32	2.03
<i>si:ch211-213a13.5</i>	si:ch211-213a13.5	1.83	2.08	2.69
<i>safb</i>	scaffold attachment factor B	1.82	1.15	1.74
<i>znf451</i>	zinc finger protein 451	1.82	0.87	1.53
<i>pnp1a7a</i>	patatin-like phospholipase domain containing 7a	1.81	0.99	1.66
<i>rreb1b</i>	ras responsive element binding protein 1b	1.81	1.10	1.92
<i>uhmk1</i>	U2AF homology motif (UHM) kinase 1	1.8	1.69	2.38
<i>znf438</i>	zinc finger protein 438	1.8	1.94	3.36
<i>mbtps2</i>	membrane-bound transcription factor peptidase, site 2	1.79	0.96	1.79
<i>wdr45</i>	WD repeat domain 45	1.79	0.97	1.42
<i>cnot6a</i>	CCR4-NOT transcription complex, subunit 6a	1.79	1.08	2.00
<i>shroom2a</i>	shroom family member 2a	1.79	1.37	3.14
<i>mtmr14</i>	myotubularin related protein 14	1.79	0.84	1.52
<i>ppp1r12c</i>	protein phosphatase 1, regulatory subunit 12C	1.78	1.37	1.93
<i>mtmr9</i>	myotubularin related protein 9	1.77	0.99	1.51
<i>cep290</i>	centrosomal protein 290	1.77	1.35	2.22
<i>wdr41</i>	WD repeat domain 41	1.77	1.43	2.04
<i>pi4k2b</i>	phosphatidylinositol 4-kinase type 2 beta	1.75	0.98	1.65
<i>dopey1</i>	dopey family member 1	1.75	1.19	2.30
<i>wipf2a</i>	WAS/WASL interacting protein family, member 2a	1.75	0.93	1.66
<i>pank2</i>	pantothenate kinase 2	1.74	1.22	1.77
<i>ankrd12</i>	ankyrin repeat domain 12	1.74	1.25	2.06
<i>tab1</i>	TGF-beta activated kinase 1/MAP3K7 binding protein 1	1.74	0.96	1.53
<i>abca3b</i>	ATP-binding cassette, sub-family A (ABC1), member 3b	1.73	0.98	1.69
<i>spg11</i>	spastic paraplegia 11	1.73	1.16	1.85
<i>cdc14b</i>	cell division cycle 14B	1.73	1.68	2.48
<i>si:dkey-97a13.6</i>	si:dkey-97a13.6	1.72	1.04	2.07
<i>carf</i>	calcium responsive transcription factor	1.72	1.49	1.96
<i>ssbp4</i>	single stranded DNA binding protein 4	1.71	1.49	3.25
<i>si:dkey-28a3.2</i>	si:dkey-28a3.2	1.7	0.99	1.73
<i>si:ch211-230g15.5</i>	si:ch211-230g15.5	1.69	1.27	2.27
<i>malt3</i>	MALT paracaspase 3	1.69	1.04	2.50
<i>im:7160594</i>	im:7160594	1.69	0.84	1.54
<i>fmnl3</i>	formin-like 3	1.68	1.19	2.03
<i>pi4kb</i>	phosphatidylinositol 4-kinase, catalytic, beta	1.66	0.95	1.80
<i>stag1a</i>	stromal antigen 1a	1.66	1.68	2.41
<i>csnk1db</i>	casein kinase 1, delta b	1.65	1.27	1.82
<i>dtnbp1a</i>	dystrobrevin binding protein 1a	1.65	1.00	1.47
<i>taf2</i>	TAF2 RNA polymerase II, TATA box binding protein (TBP)-associated factor	1.65	1.06	1.57
<i>ncoa5</i>	nuclear receptor coactivator 5	1.65	1.05	1.83

<i>usp25</i>	ubiquitin specific peptidase 25	1.65	1.16	1.69
<i>foxp1b</i>	forkhead box P1b	1.64	1.25	1.93
<i>nrbp2b</i>	nuclear receptor binding protein 2b	1.64	1.49	2.23
<i>ypel5</i>	yippee-like 5	1.63	1.14	1.42
<i>ftr79</i>	finTRIM family, member 79	1.62	1.41	2.33
<i>gpc4</i>	glypican 4	1.62	1.07	1.74
<i>si:dkey-156n14.5</i>	si:dkey-156n14.5	1.62	1.26	1.95
<i>gatsl2</i>	GATS protein-like 2	1.62	1.34	2.06
<i>phrf1</i>	PHD and ring finger domains 1	1.62	1.03	1.88
<i>trafd1</i>	TRAF-type zinc finger domain containing 1	1.61	0.99	1.84
<i>ctdsp1</i>	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 1	1.61	0.94	1.51
<i>atmin</i>	ATM interactor	1.61	1.46	2.33
<i>gnal</i>	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	1.6	1.51	2.38
<i>tjp1a</i>	tight junction protein 1a	1.6	1.25	2.16
<i>si:dkey-16p6.1</i>	si:dkey-16p6.1	1.6	1.26	1.97
<i>wdr26b</i>	WD repeat domain 26b	1.6	0.81	1.54
<i>rbm4.2</i>	RNA binding motif protein 4.2	1.58	1.06	1.55
<i>golga4</i>	golgin A4	1.58	1.01	1.47
<i>rest</i>	RE1-silencing transcription factor	1.57	1.98	3.29
<i>yy1a</i>	YY1 transcription factor a	1.57	1.01	1.52
<i>slkb</i>	STE20-like kinase b	1.57	1.55	2.30
<i>FBXO48</i>	si:dkey-202b17.4	1.56	1.12	1.40
<i>grhpra</i>	glyoxylate reductase/hydroxypyruvate reductase a	1.56	1.45	2.00
<i>traf2b</i>	Tnf receptor-associated factor 2b	1.56	1.13	1.64
<i>si:ch73-1a9.3</i>	si:ch73-1a9.3	1.54	1.19	1.60
<i>brd9</i>	bromodomain containing 9	1.53	1.01	1.44
<i>inpp5ka</i>	inositol polyphosphate-5-phosphatase Ka	1.5	0.97	1.38
<i>add3a</i>	adducin 3 (gamma) a	1.5	1.15	1.57
<i>hook2</i>	hook microtubule-tethering protein 2	1.49	0.99	1.36
<i>per3</i>	period circadian clock 3	1.48	1.30	1.73
<i>tial1</i>	TIA1 cytotoxic granule-associated RNA binding protein-like 1	1.47	1.43	1.88
<i>hnrnpm</i>	heterogeneous nuclear ribonucleoprotein M	1.47	1.07	1.55
<i>usp8</i>	ubiquitin specific peptidase 8	1.45	0.89	1.38
<i>dusp16</i>	dual specificity phosphatase 16	1.43	1.08	1.40
<i>optn</i>	optineurin	1.4	0.46	0.62
<i>psmc1a</i>	proteasome 26S subunit, ATPase 1a	1.36	0.53	0.67
<i>arid4a</i>	AT rich interactive domain 4A (RBP1-like)	1.36	1.20	1.52
<i>cdh1</i>	cadherin 1, type 1, E-cadherin (epithelial)	1.36	1.12	1.51
<i>tfb2m</i>	transcription factor B2, mitochondrial	0.76	1.00	0.70
<i>upf1</i>	upf1 regulator of nonsense transcripts homolog (yeast)	0.72	0.92	0.70
<i>tomm22</i>	translocase of outer mitochondrial membrane 22 homolog (yeast)	0.72	0.88	0.60
<i>uba3</i>	ubiquitin-like modifier activating enzyme 3	0.71	0.82	0.55
<i>rbm25b</i>	RNA binding motif protein 25b	0.71	0.95	0.74
<i>srsf5a</i>	serine/arginine-rich splicing factor 5a	0.7	0.83	0.63
<i>sestd1</i>	SEC14 and spectrin domains 1	0.7	0.73	0.53
<i>mef2cb</i>	myocyte enhancer factor 2cb	0.68	0.87	0.69

<i>azin1a</i>	antizyme inhibitor 1a	0.68	0.86	0.57
<i>oaz1b</i>	ornithine decarboxylase antizyme 1b	0.68	0.80	0.59
<i>hmgb3b</i>	high mobility group box 3b	0.67	0.98	0.64
<i>si:dkey-286j15.1</i>	si:dkey-286j15.1	0.65	0.98	0.63
<i>lcn15</i>	lipocalin 15	0.65	1.13	0.70
<i>mapkapk2a</i>	mitogen-activated protein kinase-activated protein kinase 2a	0.65	0.95	0.54
<i>tomm70a</i>	translocase of outer mitochondrial membrane 70 homolog A (S. cerevisiae)	0.65	0.94	0.59
<i>cux2b</i>	cut-like homeobox 2b	0.64	0.81	0.48
<i>smim12</i>	small integral membrane protein 12	0.63	0.75	0.48
<i>rab35b</i>	RAB35, member RAS oncogene family b	0.63	0.94	0.60
<i>adck5</i>	aarF domain containing kinase 5	0.62	0.57	0.34
<i>nde1</i>	nudE neurodevelopment protein 1	0.62	0.96	0.54
<i>rap1ab</i>	RAP1A, member of RAS oncogene family b	0.62	0.94	0.55
<i>ddx61</i>	DEAD (Asp-Glu-Ala-Asp) box helicase 61	0.62	0.90	0.55
<i>znf574</i>	zinc finger protein 574	0.62	0.76	0.55
<i>kat2a</i>	K(lysine) acetyltransferase 2A	0.61	0.82	0.55
<i>ddx19</i>	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 19 (DBP5 homolog, yeast)	0.61	0.96	0.53
<i>dolpp1</i>	dolichyldiphosphatase 1	0.61	0.91	0.61
<i>si:ch211-210c8.7</i>	si:ch211-210c8.7	0.61	1.16	0.65
<i>mt-nd6</i>	NADH dehydrogenase 6, mitochondrial	0.61	1.11	0.63
<i>timm10b</i>	translocase of inner mitochondrial membrane 10 homolog B (yeast)	0.6	1.06	0.64
<i>kdm6al</i>	lysine (K)-specific demethylase 6A, like	0.6	0.92	0.66
<i>mapre1b</i>	microtubule-associated protein, RP/EB family, member 1b	0.6	0.92	0.52
<i>lsm1</i>	LSM1, U6 small nuclear RNA associated	0.6	1.13	0.66
<i>slc51a</i>	solute carrier family 51, alpha subunit	0.6	0.96	0.53
<i>pgam1a</i>	phosphoglycerate mutase 1a	0.59	1.03	0.62
<i>si:ch211-235e9.8</i>	si:ch211-235e9.8	0.59	0.82	0.45
<i>ppa1b</i>	pyrophosphatase (inorganic) 1b	0.59	1.00	0.58
<i>pinx1</i>	PIN2/TERF1 interacting, telomerase inhibitor 1	0.58	0.95	0.52
<i>fam136a</i>	family with sequence similarity 136, member A	0.58	0.73	0.38
<i>phospho2</i>	phosphatase, orphan 2	0.58	1.05	0.59
<i>mars</i>	methionyl-tRNA synthetase	0.57	0.86	0.49
<i>hmbsa</i>	hydroxymethylbilane synthase a	0.56	0.95	0.48
<i>si:dkey-121a9.3</i>	si:dkey-121a9.3	0.56	0.92	0.49
<i>qars</i>	glutaminyl-tRNA synthetase	0.56	0.82	0.46
<i>igdcc4</i>	immunoglobulin superfamily, DCC subclass, member 4	0.56	0.67	0.46
<i>ptpn11b</i>	protein tyrosine phosphatase, non-receptor type 11, b	0.56	0.77	0.51
<i>higd1a</i>	HIG1 hypoxia inducible domain family, member 1A	0.56	1.04	0.56
<i>si:ch73-21k16.5</i>	si:ch73-21k16.5	0.56	1.06	0.54
<i>elavl1a</i>	ELAV like RNA binding protein 1a	0.55	1.06	0.55
<i>ppih</i>	peptidylprolyl isomerase H (cyclophilin H)	0.54	0.86	0.45
<i>tor3a</i>	torsin family 3, member A	0.54	0.93	0.55
<i>hprt1</i>	hypoxanthine phosphoribosyltransferase 1	0.54	0.90	0.48
<i>sigmar1</i>	sigma non-opioid intracellular receptor 1	0.54	0.94	0.50
<i>cers2b</i>	ceramide synthase 2b	0.54	0.79	0.40
<i>si:ch211-51e12.7</i>	si:ch211-51e12.7	0.53	1.22	0.69
<i>nsdhl</i>	NAD(P) dependent steroid dehydrogenase-like	0.53	1.03	0.52
<i>btaf1</i>	BTA1 RNA polymerase II, B-TFIID transcription factor-associated	0.53	1.25	0.70

<i>lgalsla</i>	lectin, galactoside-binding-like a	0.53	1.06	0.53
<i>foxo3a</i>	forkhead box O3A	0.53	0.65	0.40
<i>CDPF1</i>	si:ch211-239e6.4	0.52	1.06	0.49
<i>upp1</i>	uridine phosphorylase 1	0.52	0.76	0.53
<i>nt5dc3</i>	5'-nucleotidase domain containing 3	0.52	0.94	0.51
<i>pus10</i>	pseudouridylate synthase 10	0.52	0.96	0.50
<i>atp13a3</i>	ATPase 13A3	0.51	0.47	0.23
<i>ccnt2b</i>	cyclin T2b	0.5	0.97	0.48
<i>slc19a2</i>	solute carrier family 19 (thiamine transporter), member 2	0.5	0.97	0.40
<i>srd5a1</i>	steroid-5-alpha-reductase, alpha polypeptide 1 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 1)	0.49	0.87	0.40
<i>ABCF3</i>	ATP binding cassette subfamily F member 3	0.49	0.75	0.38
<i>znrd1</i>	zinc ribbon domain containing 1	0.49	0.87	0.47
<i>elf4e1c</i>	eukaryotic translation initiation factor 4E family member 1c	0.49	1.01	0.48
<i>cyb5b</i>	cytochrome b5 type B	0.49	1.06	0.40
<i>cyb5r2</i>	cytochrome b5 reductase 2	0.48	0.86	0.38
<i>grtp1a</i>	growth hormone regulated TBC protein 1a	0.47	0.58	0.29
<i>nudt3b</i>	nudix (nucleoside diphosphate linked moiety X)-type motif 3b	0.47	0.74	0.39
<i>znf1007</i>	zinc finger protein 1007	0.47	0.93	0.55
<i>sema4ba</i>	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4Ba	0.47	0.75	0.33
<i>CABZ01002690.1</i>		0.46	0.74	0.37
<i>xpo4</i>	exportin 4	0.45	1.16	0.43
<i>rin2</i>	Ras and Rab interactor 2	0.45	0.92	0.44
<i>ptges3b</i>	prostaglandin E synthase 3b (cytosolic)	0.44	1.07	0.43
<i>myo10l3</i>	myosin X-like 3	0.44	0.72	0.38
<i>tim50</i>	translocase of inner mitochondrial membrane 50 homolog (S. cerevisiae)	0.44	1.02	0.41
<i>spag1a</i>	sperm associated antigen 1a	0.44	0.58	0.27
<i>gpam</i>	glycerol-3-phosphate acyltransferase, mitochondrial	0.43	0.71	0.30
<i>rpz2</i>	rapunzel 2	0.43	1.11	0.49
<i>asmt2</i>	acetylserotonin O-methyltransferase 2	0.42	0.52	0.36
<i>hs3st3b1b</i>	heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1b	0.42	0.84	0.50
<i>arhgef2</i>	rho/rac guanine nucleotide exchange factor (GEF) 2	0.4	0.87	0.28
<i>pacs2</i>	phosphofurin acidic cluster sorting protein 2	0.4	0.50	0.30
<i>NC_002333.19</i>		0.39	0.94	0.46
<i>rbp7a</i>	retinol binding protein 7a, cellular	0.39	0.54	0.18
<i>frya</i>	furry homolog a (Drosophila)	0.38	0.49	0.20
<i>aacs</i>	acetoacetyl-CoA synthetase	0.37	0.65	0.22
<i>si:ch211-197l9.2</i>	si:ch211-197l9.2	0.37	0.31	0.13
<i>dhh</i>	desert hedgehog	0.37	1.02	0.45
<i>kirrel3l</i>	kirre like nephrin family adhesion molecule 3, like	0.36	1.27	0.37
<i>calcr1b</i>	calcitonin receptor-like b	0.36	1.24	0.58
<i>ptp4a3</i>	protein tyrosine phosphatase type IVA, member 3	0.36	0.83	0.31
<i>gtf3c2</i>	general transcription factor IIIC, polypeptide 2, beta	0.35	0.94	0.43
<i>dcbl1</i>	discoidin, CUB and LCCL domain containing 1	0.34	0.38	0.13
<i>slc38a3a</i>	solute carrier family 38, member 3a	0.34	0.99	0.36
<i>idi1</i>	isopentenyl-diphosphate delta isomerase 1	0.34	1.17	0.31
<i>si:ch1073-296i8.2</i>	si:ch1073-296i8.2	0.33	0.83	0.15

<i>CABZ01015475.1</i>		0.33	1.09	0.41
<i>rbms2b</i>	RNA binding motif, single stranded interacting protein 2b	0.27	1.69	0.41
<i>gramd4a</i>	GRAM domain containing 4a	0.27	1.49	0.40
<i>NC_002333.2</i>		0.27	0.38	0.13
<i>ebp</i>	emopamil binding protein (sterol isomerase)	0.26	1.12	0.22
<i>fdft1</i>	farnesyl-diphosphate farnesyltransferase 1	0.26	1.25	0.27
<i>hsd17b7</i>	hydroxysteroid (17-beta) dehydrogenase 7	0.26	1.37	0.34
<i>fgf13b</i>	fibroblast growth factor 13b	0.25	0.52	0.12
<i>mvda</i>	mevalonate (diphospho) decarboxylase a	0.25	1.35	0.26
<i>msmo1</i>	methylsterol monooxygenase 1	0.23	1.89	0.31
<i>sqlea</i>	squalene epoxidase a	0.18	1.88	0.16
<i>bach2a</i>	BTB and CNC homology 1, basic leucine zipper transcription factor 2a	0.18	0.57	0.17
<i>lss</i>	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	0.17	1.19	0.14
<i>mvk</i>	mevalonate kinase	0.16	1.81	0.28
<i>hmgcs1</i>	3-hydroxy-3-methylglutaryl-CoA synthase 1 (soluble)	0.15	1.44	0.16
<i>fdps</i>	farnesyl diphosphate synthase (farnesyl pyrophosphate synthetase, dimethylallyltranstransferase, geranyltranstransferase)	0.14	2.39	0.27
<i>igsf9ba</i>	immunoglobulin superfamily, member 9Ba	0.12	1.71	0.33
<i>rpp25a</i>	ribonuclease P and MRP subunit p25, a	0.1	1.97	0.12
<i>zbtb16a</i>	zinc finger and BTB domain containing 16a	0.07	1.05	0.09

Table S2. List of DEPs identified from LC-MS/MS

Gene	Product	Z+/A+	A+/A-	Z+/Z-
Scgn	secretagogen, EF-hand calcium binding protein	9.89	1.18	2.76
Mgst2	microsomal glutathione S-transferase 2	5.18	0.52	3.52
GFP-T2A-AAT-transgene	GFP-T2A-AAT-transgene	4.63	1.02	5.59
Sdsl	serine dehydratase-like	3.43	2.98	1.93
Liph	lipase member H	3.13	0.70	5.05
Vmo1a	vitelline membrane outer layer 1 homolog a	2.77	1.52	1.95
Lrp1aa	low density lipoprotein receptor-related protein 1Aa	2.36	0.79	1.16
Si:ch211-74f19.2	si:ch211-74f19.2	1.95	0.71	2.42
Mpdu1b	mannose-P-dolichol utilization defect 1b	1.93	0.79	1.26
Fuk	fucokinase	1.65	0.86	1.09
Caska	calcium/calmodulin-dependent serine protein kinase a	1.64	0.79	1.52
Psmg1	proteasome (prosome, macropain) assembly chaperone 1	1.55	0.52	0.84
Sccpdhb	saccharopine dehydrogenase b	1.54	0.84	1.12
Larp4aa	La ribonucleoprotein domain family, member 4Aa	1.52	0.47	0.73
Mipep	mitochondrial intermediate peptidase	1.5	0.87	1.27
Anxa11b	annexin A11b	1.48	0.99	1.64
Sil1	SIL1 nucleotide exchange factor	1.45	0.48	0.86
Rrbp1b	ribosome binding protein 1b	1.43	0.23	0.55
Farsa	phenylalanyl-tRNA synthetase, alpha subunit	1.43	0.58	0.69
Zgc:152945	zgc:152945	1.41	0.40	0.73
Pcyt2	phosphate cytidyltransferase 2, ethanolamine	1.4	0.53	0.76
Apobb.2	apolipoprotein Bb, tandem duplicate 2	1.38	0.88	1.41
Ipo7	importin 7	1.36	0.71	0.71
Setd1a	SET domain containing 1A	1.33	0.47	0.73
Erlec1	endoplasmic reticulum lectin 1	1.32	0.63	0.71
Dpm3	dolichyl-phosphate mannosyltransferase polypeptide 3	1.31	0.58	0.46
Larsa	leucyl-tRNA synthetase a	1.3	0.60	0.79
Rock2a	rho-associated, coiled-coil containing protein kinase 2a	1.29	0.85	1.43
Memo1	mediator of cell motility 1	1.29	0.74	0.83
Rab1ab	RAB1A, member RAS oncogene family b	1.27	0.62	0.84
Tmem177	transmembrane protein 177	1.27	0.97	1.31
Zgc:101540	zgc:101540	1.26	0.95	1.57
C8b	complement component 8, beta polypeptide	1.25	0.93	1.46
Fam3a	family with sequence similarity 3, member A	1.25	0.73	0.82
Abraxas2b	abraxas 2b, BRISC complex subunit	1.23	1.02	1.14
Sec61b	Sec61 translocon beta subunit	1.23	0.71	0.59
Vcp	valosin containing protein	1.22	0.67	0.74
Drg1	developmentally regulated GTP binding protein 1	1.21	0.70	0.81
Slc16a2	solute carrier family 16 member 2	1.2	0.80	0.78
Ufl1	UFM1-specific ligase 1	1.2	0.79	0.73
Gspt1l	G1 to S phase transition 1, like	1.19	0.70	0.76
Rab1aa	RAB1A, member RAS oncogene family a	1.19	0.70	0.85
Psm2	proteasome subunit alpha 2	1.17	0.80	0.85
Slc23a1	solute carrier family 23 (ascorbic acid transporter), member 1	1.15	1.00	1.15
Pafah1b1a	platelet-activating factor acetylhydrolase 1b, regulatory subunit 1a	1.13	0.81	0.87

Rab5c	RAB5C, member RAS oncogene family	1.12	0.80	0.94
Ufd1l	ubiquitin recognition factor in ER associated degradation 1	1.11	0.86	0.82
Psmc7	proteasome 26S subunit, non-ATPase 7	1.09	0.90	0.83
Mest	mesoderm specific transcript	0.9	1.06	0.93
Tmed7	transmembrane p24 trafficking protein 7	0.87	0.93	0.93
Cfl1	cofilin 1	0.86	1.03	0.88
Erp44	endoplasmic reticulum protein 44	0.84	0.95	0.85
Srsf5b	serine/arginine-rich splicing factor 5b	0.82	1.15	0.85
Enpp1	ectonucleotide pyrophosphatase/phosphodiesterase 1	0.82	1.55	1.58
Pyroxd2	pyridine nucleotide-disulphide oxidoreductase domain 2	0.82	1.05	0.90
Slc12a4	solute carrier family 12 (potassium/chloride transporter), member 4	0.81	1.06	0.79
Im:7138535	im:7138535	0.8	1.15	0.83
Dpy19l1	dpy-19-like 1, like (H. sapiens)	0.8	1.73	1.21
Cct2	haperonin containing TCP1 complex subunit 2	0.78	1.31	1.24
Gale	UDP-galactose-4-epimerase	0.76	1.23	0.81
Epcam	epithelial cell adhesion molecule	0.75	0.90	0.71
Snrpd3l	small nuclear ribonucleoprotein D3 polypeptide, like	0.74	0.93	0.61
Aldh9a1a	aldehyde dehydrogenase 9 family, member A1a	0.71	1.22	0.95
Rdh14b	retinol dehydrogenase 14b	0.69	1.17	0.84
Gpa33	glycoprotein A33 (transmembrane)	0.68	1.04	0.52
Mgc173689	MGC: 173689	0.63	0.93	0.78
Coro1a	coronin, actin binding protein, 1A	0.6	0.93	0.60
Krt91	keratin 91	0.57	1.20	0.70
Zgc:103586	zgc:103586	0.57	1.54	0.84
Tcea3	transcription elongation factor A (SII), 3	0.53	0.97	0.49
Ckmb	creatine kinase, muscle b	0.48	1.09	0.46
Nudt7	nudix (nucleoside diphosphate linked moiety X)-type motif 7	0.46	0.78	0.37
Zgc:174259	zgc:174259	0.38	0.87	0.45
Dap1b	death associated protein 1b	0.37	1.31	0.29
Pla2g1b	phospholipase A2, group IB (pancreas)	0.36	3.65	0.15
Pck1	phosphoenolpyruvate carboxykinase 1 (soluble)	0.35	0.72	0.18
Si:ch1073-110a20.3	si:ch1073-110a20.3	0.28	1.51	0.21

Table S3. GO enrichment from RNA-seq DEGs

	Gene Ontology Term (GO term)	Enrichment score
1	Response To Purine-Containing Compound	34.711
2	Isoprenoid Biosynthetic Process	30.819
3	Cholesterol Biosynthetic Process	30.639
4	Regulation Of Endosome Size	29.2
5	Autophagy Of Host Cells Involved In Interaction With Symbiont	27.769
6	Regulation Of Cholesterol Biosynthetic Process	25.244
7	Isopentenyl Diphosphate Biosynthetic Process, Mevalonate Pathway	19.467
8	Positive Regulation Of Rac Protein Signal Transduction	19.467
9	Positive Regulation Of Transcription From Rna Polymerase Ii Promoter Involved In Unfolded Protein Response	19.467
10	Glycerol-3-Phosphate Metabolic Process	19.467
11	Sterol Biosynthetic Process	16.686
12	Positive Regulation Of Protein Homodimerization Activity	15.427
13	Positive Regulation Of Hydrogen Peroxide-Mediated Programmed Cell Death	14.6
14	Negative Regulation Of Activation-Induced Cell Death Of T Cells	14.6
15	Regulation Of Autophagy	13.017
16	Receptor Recycling	12.622
17	Regulation Of Androgen Receptor Signaling Pathway	12.622
18	Cellular Response To Nerve Growth Factor Stimulus	12.24
19	Protein Localization	11.733
20	Dolichyl Diphosphate Biosynthetic Process	11.68
21	Positive Regulation Of Chromosome Segregation	11.68
22	Parkin-Mediated Stimulation Of Mitophagy In Response To Mitochondrial Depolarization	11.68
23	Regulation Of Establishment Of Protein Localization	11.68
24	Regulation Of Kinase Activity	11.68
25	Internal Peptidyl-Lysine Acetylation	11.68
26	Regulation Of Fatty Acid Metabolic Process	11.68
27	Liver Development	11.412
28	Phosphatidylinositol Biosynthetic Process	11.124
29	Positive Regulation Of Microtubule Polymerization	10.157
30	Regulation Of Rho Protein Signal Transduction	10.037
31	Peptidyl-Tyrosine Dephosphorylation	9.898
32	Optic Nerve Development	9.733
33	Regulation Of Phosphatidylinositol Dephosphorylation	9.733
34	Response To Fungicide	9.733
35	Regulation Of Tumor Necrosis Factor Production	9.733
36	Cytoplasmic Microtubule Organization	9.636
37	Response To Starvation	9.417
38	Negative Regulation Of Protein Complex Assembly	9.256
39	Histone H3-K9 Demethylation	9.256
40	Axon Extension	8.985
41	Establishment Of Endothelial Barrier	8.678
42	Negative Regulation Of Collateral Sprouting	8.343
43	Protein K63-Linked Deubiquitination	8.343
44	Microtubule Severing	8.343
45	Plus-End-Directed Vesicle Transport Along Microtubule	8.343
46	Insulin Secretion Involved In Cellular Response To Glucose Stimulus	8.343
47	Positive Regulation Of Receptor Biosynthetic Process	8.343
48	Negative Regulation Of Interferon-Gamma-Mediated Signaling Pathway	8.343
49	Regulation Of Protein Export From Nucleus	8.343
50	Regulation Of Circadian Sleep/Wake Cycle, Sleep	8.343
51	Regulation Of Cellular Amino Acid Metabolic Process	8.343

52	Autophagosome Assembly	8.234
53	Autophagy	8.22
54	Microtubule Nucleation	7.308
55	Platelet Formation	7.308
56	Neuron Projection Regeneration	7.3
57	Negative Regulation Of B Cell Apoptotic Process	7.3
58	Regulation Of Dendritic Spine Development	7.3
59	Cellular Response To Testosterone Stimulus	7.3
60	Negative Regulation Of Type I Interferon-Mediated Signaling Pathway	7.3
61	Entry Of Bacterium Into Host Cell	7.3
62	Death-Inducing Signaling Complex Assembly	7.3
63	Protein Targeting To Mitochondrion	6.871
64	Establishment Of Protein Localization To Membrane	6.489
65	Histone H2B Ubiquitination	6.489
66	Regulation Of Glucose Import	6.489
67	Dephosphorylation	6.376
68	Phosphatidylinositol Dephosphorylation	6.311
69	Entrainment Of Circadian Clock By Photoperiod	6.311
70	Circadian Regulation Of Gene Expression	6.164
71	Endosome Organization	6.147
72	Establishment Of Mitotic Spindle Orientation	6.037
73	Deadenylation-Dependent Decapping Of Nuclear-Transcribed Mrna	5.84
74	Intraciliary Transport Involved In Cilium Assembly	5.84
75	Response To Uv-C	5.84
76	Histone H3-K36 Demethylation	5.84
77	Positive Regulation Of Transcription, Dna-Templated	5.8
78	Negative Regulation Of Microtubule Depolymerization	5.785
79	Positive Regulation Of Extrinsic Apoptotic Signaling Pathway	5.785
80	Protein Autophosphorylation	5.774
81	Negative Regulation Of Neuron Differentiation	5.65
82	Regulation Of Megakaryocyte Differentiation	5.562
83	Fatty Acid Metabolic Process	5.557
84	Protein Phosphorylation	5.359
85	Steroid Biosynthetic Process	5.34
86	Microtubule Bundle Formation	5.34
87	Cellular Response To Insulin Stimulus	5.328
88	Cellular Response To Nutrient Levels	5.309
89	Positive Regulation Of Autophagosome Assembly	5.309
90	Rap Protein Signal Transduction	5.309
91	Positive Regulation Of Nuclear-Transcribed Mrna Poly(A) Tail Shortening	5.309
92	Cell-Cell Junction Assembly	5.309
93	Cyclooxygenase Pathway	5.309
94	Gene Silencing By Mirna	5.309
95	Regulation Of Stem Cell Population Maintenance	5.309
96	Mitochondrial Transcription	5.309
97	Transcription By Rna Polymerase Ii	5.302
98	Cholesterol Metabolic Process	5.215
99	Macroautophagy	5.206
100	Activation Of Protein Kinase Activity	4.977
101	Protein Deubiquitination	4.965
102	Regulation Of Tumor Necrosis Factor-Mediated Signaling Pathway	4.959
103	Regulation Of Circadian Rhythm	4.867
104	Histone Monoubiquitination	4.867
105	White Fat Cell Differentiation	4.867
106	Mrna Cleavage	4.867

107	Regulation Of Histone Methylation	4.867
108	Negative Regulation By Host Of Viral Transcription	4.867
109	Regulation Of Protein Stability	4.843
110	Neuron Projection Development	4.782
111	Protein K48-Linked Deubiquitination	4.628
112	Regulation Of Gene Expression	4.591
113	Cellular Response To Hormone Stimulus	4.58
114	Cellular Response To Cholesterol	4.492
115	Peptidyl-Serine Phosphorylation	4.492
116	Protein Neddylation	4.492
117	Protein Localization To Phagophore Assembly Site	4.492
118	Covalent Chromatin Modification	4.492
119	Wnt Signaling Pathway	4.479
120	Cellular Response To Dexamethasone Stimulus	4.479
121	Positive Regulation Of Transcription By Rna Polymerase Ii	4.447
122	Cellular Response To Camp	4.408
123	Positive Regulation Of Protein Kinase Activity	4.408
124	Positive Regulation Of Neuron Differentiation	4.346
125	Anterograde Axonal Transport	4.339
126	Positive Regulation Of Gene Expression, Epigenetic	4.339
127	Negative Regulation Of Insulin Receptor Signaling Pathway	4.339
128	Glucose Homeostasis	4.313
129	Cell Proliferation	4.241
130	Nucleobase-Containing Compound Metabolic Process	4.207
131	3'-Utr-Mediated Mrna Destabilization	4.171
132	Positive Regulation Of Nuclear-Transcribed Mrna Catabolic Process, Deadenylation-Dependent Decay	4.171
133	Prostaglandin Biosynthetic Process	4.171
134	Protein Polyubiquitination	4.145
135	Spermatid Development	4.134
136	Locomotory Behavior	4.134
137	Cell Death	4.084
138	Response To Nutrient Levels	4.084
139	Positive Regulation Of Apoptotic Process	4.079
140	In Utero Embryonic Development	4.074
141	Oxidation-Reduction Process	3.985
142	Brain Development	3.967
143	Positive Regulation Of Epithelial Cell Migration	3.967
144	Negative Regulation Of Extrinsic Apoptotic Signaling Pathway Via Death Domain Receptors	3.967
145	Cellular Response To Glucose Stimulus	3.959
146	Protein Dephosphorylation	3.93
147	Neuromuscular Process	3.893
148	Positive Regulation Of Keratinocyte Differentiation	3.893
149	Negative Regulation Of Neurogenesis	3.893
150	Megakaryocyte Development	3.893
151	Chromosome Organization	3.893
152	Histone Mrna Catabolic Process	3.893
153	Endocytosis	3.877
154	Trna Aminoacylation For Protein Translation	3.857
155	Positive Regulation Of Gtpase Activity	3.772
156	Negative Regulation Of Transcription By Rna Polymerase Ii	3.769
157	G2/M Transition Of Mitotic Cell Cycle	3.743
158	Protein Ubiquitination	3.72
159	Response To Estrogen	3.708
160	Regulation Of Mitotic Cell Cycle	3.685
161	Phosphatidic Acid Biosynthetic Process	3.654

162	Regulation Of Macroautophagy	3.65
163	Vascular Endothelial Growth Factor Receptor Signaling Pathway	3.65
164	Stimulatory C-Type Lectin Receptor Signaling Pathway	3.65
165	Alternative Mrna Splicing, Via Spliceosome	3.65
166	Signal Transduction	3.646
167	Smoothed Signaling Pathway	3.594
168	Protein Destabilization	3.471
169	Intracellular Receptor Signaling Pathway	3.471
170	Cellular Response To Epidermal Growth Factor Stimulus	3.471
171	Protein Localization To Plasma Membrane	3.457
172	Positive Regulation Of Histone Acetylation	3.435
173	Ras Protein Signal Transduction	3.435
174	Camera-Type Eye Morphogenesis	3.435
175	Negative Regulation Of Transcription, Dna-Templated	3.429
176	Cellular Response To Glucose Starvation	3.386
177	Transcription Initiation From Rna Polymerase Ii Promoter	3.336
178	Phosphorylation	3.324
179	Chromatin Remodeling	3.324
180	Regulation Of Cilium Assembly	3.306
181	Non-Motile Cilium Assembly	3.306
182	Regulation Of Actin Cytoskeleton Reorganization	3.244
183	Chromosome Segregation	3.244
184	Apoptotic Cell Clearance	3.244
185	Positive Regulation Of Transcription Of Notch Receptor Target	3.244
186	Regulation Of Neuron Apoptotic Process	3.244
187	3'-Utr-Mediated Mrna Stabilization	3.244
188	Regulation Of Cellular Response To Heat	3.229
189	Regulation Of Synaptic Plasticity	3.156
190	Transcription, Dna-Templated	3.132
191	Response To Toxic Substance	3.115
192	Actin Cytoskeleton Organization	3.102
193	Regulation Of Catalytic Activity	3.085
194	Endoplasmic Reticulum Unfolded Protein Response	3.085
195	Mrna Stabilization	3.074
196	Histone H3 Deacetylation	3.074
197	Negative Regulation Of Rho Protein Signal Transduction	3.074
198	Triglyceride Biosynthetic Process	3.074
199	Protein Localization To Golgi Apparatus	3.074
200	Multicellular Organism Development	3.056
201	Mapk Cascade	3.047
202	Ubiquitin-Dependent Protein Catabolic Process	3.021
203	Rna Secondary Structure Unwinding	3.018
204	Androgen Receptor Signaling Pathway	3.018
205	Cellular Response To Cytokine Stimulus	3.018
206	Heart Development	2.958
207	Positive Regulation Of Stress Fiber Assembly	2.954
208	Cell Cycle	2.954
209	Dna Duplex Unwinding	2.954
210	Skeletal Muscle Tissue Development	2.954
211	Negative Regulation Of Inflammatory Response	2.92
212	Positive Regulation Of Protein Export From Nucleus	2.92
213	Circadian Rhythm	2.92
214	Negative Regulation Of Stress Fiber Assembly	2.92
215	Protein Import Into Mitochondrial Matrix	2.92
216	Neurotrophin Trk Receptor Signaling Pathway	2.92

217	Nervous System Development	2.904
218	Double-Strand Break Repair Via Homologous Recombination	2.884
219	Insulin Receptor Signaling Pathway	2.849
220	Regulation Of G2/M Transition Of Mitotic Cell Cycle	2.849
221	Protein Stabilization	2.813
222	Regulation Of Mitotic Spindle Assembly	2.781
223	Rac Protein Signal Transduction	2.781
224	B Cell Homeostasis	2.781
225	Negative Regulation Of Protein Serine/Threonine Kinase Activity	2.781
226	Response To Light Stimulus	2.781
227	Positive Regulation Of Intracellular Protein Transport	2.781
228	Negative Regulation Of Gene Expression	2.778
229	Phosphatidylinositol-3-Phosphate Biosynthetic Process	2.777
230	Cell Division	2.74
231	Negative Regulation Of Canonical Wnt Signaling Pathway	2.734
232	Regulation Of Vesicle Fusion	2.722
233	Somatic Stem Cell Population Maintenance	2.722
234	Regulation Of Transcription, Dna-Templated	2.679
235	Nucleotide-Binding Oligomerization Domain Containing Signaling Pathway	2.655
236	Telomere Maintenance Via Telomerase	2.655
237	Melanosome Organization	2.655
238	Mrna Processing	2.633
239	Regulation Of Lipid Metabolic Process	2.625
240	Positive Regulation Of Smooth Muscle Cell Proliferation	2.62
241	Hemopoiesis	2.571
242	Negative Regulation Of Catalytic Activity	2.571
243	Cell Morphogenesis	2.567
244	Activation Of Gtpase Activity	2.539
245	Cellular Response To Glucocorticoid Stimulus	2.539
246	Dna Methylation	2.539
247	Lipid Metabolic Process	2.53
248	Protein Autoubiquitination	2.524
249	Small Gtpase Mediated Signal Transduction	2.512
250	Cellular Response To Drug	2.479
251	Defense Response To Virus	2.475
252	Ciliary Basal Body-Plasma Membrane Docking	2.459
253	Signal Transduction By Protein Phosphorylation	2.436
254	Positive Regulation Of Defense Response To Virus By Host	2.433
255	Mrna Export From Nucleus	2.408
256	Regulation Of Small Gtpase Mediated Signal Transduction	2.404
257	Heart Looping	2.394
258	Intracellular Signal Transduction	2.36
259	Regulation Of Transcription By Rna Polymerase Ii	2.329
260	Apoptotic Process	2.297
261	Double-Strand Break Repair	2.276
262	Neuron Migration	2.268
263	Negative Regulation Of Protein Kinase Activity	2.246
264	Neuron Projection Morphogenesis	2.239
265	Mitotic Cytokinesis	2.239
266	Regulation Of Translation	2.239
267	Regulation Of Alternative Mrna Splicing, Via Spliceosome	2.239
268	Cilium Assembly	2.22
269	Intracellular Protein Transport	2.204
270	Regulation Of Cell Cycle	2.204
271	Protein Homooligomerization	2.199

272	Regulation Of Insulin Secretion	2.169
273	Positive Regulation Of Protein Binding	2.169
274	Phospholipid Biosynthetic Process	2.163
275	Regulation Of Transcription From Rna Polymerase Ii Promoter In Response To Hypoxia	2.163
276	Pituitary Gland Development	2.163
277	I-Kappab Kinase/Nf-Kappab Signaling	2.136
278	Peptidyl-Tyrosine Phosphorylation	2.132
279	Dna Repair	2.106
280	Adipose Tissue Development	2.086
281	Synaptic Transmission, Glutamatergic	2.086
282	Bile Acid And Bile Salt Transport	2.086
283	Limb Development	2.086
284	Endocytic Recycling	2.086
285	Protein Homotrimerization	2.086
286	Negative Regulation Of Insulin Secretion	2.086
287	Golgi To Plasma Membrane Protein Transport	2.086
288	Regulation Of Cell Shape	2.08
289	Phosphatidylinositol Phosphorylation	2.067
290	Protein-Containing Complex Assembly	2.031
291	Active Evasion Of Host Immune Response Via Regulation Of Host Antigen Processing And Presentation	2.014
292	Beta-Catenin-Tcf Complex Assembly	2.014
293	Negative Regulation Of Type I Interferon Production	2.014
294	Endothelial Cell Migration	2.014
295	Positive Regulation Of Protein Import Into Nucleus	2.014
296	Neuromuscular Junction Development	2.014
297	Glycogen Metabolic Process	2.014
298	Cell Differentiation	1.997
299	Notch Signaling Pathway	1.997
300	Activation Of Mapk Activity	1.997
301	Cellular Response To Dna Damage Stimulus	1.986
302	Regulation Of Gtpase Activity	1.983
303	Regulation Of Mitochondrial Membrane Potential	1.947
304	Positive Regulation Of Tor Signaling	1.947
305	Positive Regulation Of Smoothed Signaling Pathway	1.947
306	Hippo Signaling	1.947
307	Extrinsic Apoptotic Signaling Pathway In Absence Of Ligand	1.947
308	Rab Protein Signal Transduction	1.928
309	Positive Regulation Of Gene Expression	1.919
310	Positive Regulation Of Glucose Import	1.884
311	Rna Phosphodiester Bond Hydrolysis, Exonucleolytic	1.884
312	Dna Damage Checkpoint	1.884
313	Behavioral Fear Response	1.884
314	Dorsal/Ventral Pattern Formation	1.884
315	Positive Regulation Of Mitotic Cell Cycle	1.884
316	Peptidyl-Threonine Phosphorylation	1.876
317	Response To Endoplasmic Reticulum Stress	1.876
318	Dna Recombination	1.876
319	Protein Transport	1.844
320	Positive Regulation Of Proteasomal Ubiquitin-Dependent Protein Catabolic Process	1.827
321	Lipid Homeostasis	1.825
322	Regulation Of Rna Splicing	1.825
323	Mrna Splicing, Via Spliceosome	1.819
324	Cellular Response To Calcium Ion	1.803
325	Negative Regulation Of Cell Proliferation	1.783
326	Endosomal Transport	1.78

327	Fibroblast Growth Factor Receptor Signaling Pathway	1.78
328	Negative Regulation Of Tor Signaling	1.77
329	Histone H4 Acetylation	1.77
330	Exonucleolytic Nuclear-Transcribed Mrna Catabolic Process Involved In Deadenylation-Dependent Decay	1.77
331	Positive Regulation Of Telomerase Activity	1.718
332	Stress-Activated Protein Kinase Signaling Cascade	1.718
333	Liver Regeneration	1.718
334	Multicellular Organism Growth	1.714
335	Regulation Of Signal Transduction By P53 Class Mediator	1.714
336	Sensory Perception Of Sound	1.681
337	Positive Regulation Of Peptidyl-Serine Phosphorylation	1.673
338	Rho Protein Signal Transduction	1.673
339	Long-Term Memory	1.669
340	Cellular Response To Estradiol Stimulus	1.669
341	Post-Translational Protein Modification	1.668
342	Positive Regulation Of Nf-Kappab Transcription Factor Activity	1.645
343	Sodium Ion Transport	1.633
344	Response To Organic Substance	1.622
345	Semaphorin-Plexin Signaling Pathway	1.622
346	Histone Acetylation	1.622
347	Dendrite Morphogenesis	1.622
348	Regulation Of Apoptotic Process	1.584
349	Positive Regulation Of Jun Kinase Activity	1.578
350	Hair Follicle Development	1.578
351	Cell Migration	1.555
352	Positive Regulation Of Protein Phosphorylation	1.547
353	Glycosaminoglycan Biosynthetic Process	1.537
354	Negative Regulation Of G0 To G1 Transition	1.537
355	Cellular Response To Leukemia Inhibitory Factor	1.526
356	Male Gonad Development	1.509
357	Fertilization	1.497
358	Chondrocyte Differentiation	1.497
359	Sodium Ion Transmembrane Transport	1.493
360	Negative Regulation Of Signal Transduction	1.477
361	Angiogenesis	1.474
362	Positive Regulation Of Erk1 And Erk2 Cascade	1.474
363	Regulation Of Endocytosis	1.46
364	Regulation Of Cytokinesis	1.46
365	Scf-Dependent Proteasomal Ubiquitin-Dependent Protein Catabolic Process	1.46
366	Spermatogenesis	1.453
367	Transmembrane Transport	1.436
368	Cytoskeleton Organization	1.433
369	Positive Regulation Of B Cell Proliferation	1.424
370	Steroid Metabolic Process	1.424
371	Negative Regulation Of Autophagy	1.424
372	Positive Regulation Of Autophagy	1.424
373	Negative Regulation Of Protein Kinase B Signaling	1.424
374	Autophagy Of Mitochondrion	1.424
375	Bone Development	1.39
376	Erythrocyte Differentiation	1.39
377	Actin Filament Bundle Assembly	1.39
378	Rna Splicing	1.374
379	Positive Regulation Of Insulin Secretion	1.358
380	Phosphatidylinositol-Mediated Signaling	1.358
381	Viral Process	1.348

382	Platelet Activation	1.335
383	Histone H3 Acetylation	1.327
384	Activation Of Mapkk Activity	1.327
385	Rna Metabolic Process	1.327
386	Anatomical Structure Development	1.298
387	Endosome To Lysosome Transport	1.298
388	Inner Ear Development	1.298
389	Negative Regulation Of Neuron Death	1.298
390	Cell-Cell Adhesion	1.298
391	Positive Regulation Of Protein Serine/Threonine Kinase Activity	1.27
392	Calcium-Dependent Cell-Cell Adhesion Via Plasma Membrane Cell Adhesion Molecules	1.27
393	Response To Organic Cyclic Compound	1.27
394	Positive Regulation Of Dna Binding Transcription Factor Activity	1.262
395	Positive Regulation Of Cysteine-Type Endopeptidase Activity Involved In Apoptotic Process	1.243
396	Inositol Phosphate Metabolic Process	1.243
397	Gluconeogenesis	1.243
398	Negative Regulation Of Protein Ubiquitination	1.243
399	Regulation Of Signal Transduction	1.243
400	Histone Deacetylation	1.217
401	Microtubule-Based Movement	1.197
402	Neutrophil Degranulation	1.193
403	Positive Regulation Of Fat Cell Differentiation	1.192
404	Response To Cytokine	1.192
405	Receptor-Mediated Endocytosis	1.18
406	Calcium Ion Transmembrane Transport	1.177
407	Positive Regulation Of Nik/Nf-Kappab Signaling	1.168
408	Learning Or Memory	1.168
409	Phagocytosis	1.168
410	Positive Regulation Of Mapk Cascade	1.147
411	Interleukin-1-Mediated Signaling Pathway	1.145
412	Somitogenesis	1.145
413	Cellular Response To Uv	1.145
414	T Cell Costimulation	1.145
415	Spindle Assembly	1.145
416	Cellular Response To Tumor Necrosis Factor	1.138
417	Steroid Hormone Mediated Signaling Pathway	1.102
418	Dna Replication	1.093
419	Proteolysis	1.093
420	Cellular Response To Transforming Growth Factor Beta Stimulus	1.081
421	Regulation Of Mapk Cascade	1.081
422	Chromatin Organization	1.076
423	Negative Regulation Of Phosphatase Activity	1.062
424	Mrna 3'-End Processing	1.062
425	Cell-Cell Signaling	1.046
426	Glucose Metabolic Process	1.043
427	Dna Damage Response, Signal Transduction By P53 Class Mediator Resulting In Cell Cycle Arrest	1.043
428	Retinoid Metabolic Process	1.025
429	Negative Regulation Of Epithelial Cell Proliferation	1.025
430	Embryonic Digit Morphogenesis	1.007
431	Cartilage Development	1.007

Table S4. KEGG enrichment from RNA-seq DEGs

	KEGG pathway	Enrichment score
1	Steroid Biosynthesis	42.482
2	Terpenoid Backbone Biosynthesis	17.748
3	Longevity Regulating Pathway	12.553
4	Renal Cell Carcinoma	9.578
5	Ampk Signaling Pathway	9.31
6	Inositol Phosphate Metabolism	8.931
7	Circadian Rhythm	8.679
8	Parathyroid Hormone Synthesis, Secretion And Action	7.615
9	Phosphatidylinositol Signaling System	6.676
10	Autophagy - Animal	6.306
11	Mitophagy - Animal	6.007
12	Hedgehog Signaling Pathway	5.725
13	Thyroid Hormone Signaling Pathway	5.698
14	Adipocytokine Signaling Pathway	5.659
15	Notch Signaling Pathway	5.605
16	Neurotrophin Signaling Pathway	5.554
17	Adherens Junction	5.423
18	Bacterial Invasion Of Epithelial Cells	5.276
19	Metabolic Pathways	5.187
20	Glucagon Signaling Pathway	5.064
21	Insulin Resistance	4.875
22	Viral Carcinogenesis	4.774
23	Vegf Signaling Pathway	4.56
24	Herpes Simplex Infection	4.363
25	Central Carbon Metabolism In Cancer	4.139
26	Focal Adhesion	4.056
27	Long-Term Potentiation	4.016
28	Foxo Signaling Pathway	3.952
29	Tight Junction	3.888
30	Estrogen Signaling Pathway	3.807
31	Mapk Signaling Pathway	3.787
32	Vasopressin-Regulated Water Reabsorption	3.634
33	Leukocyte Transendothelial Migration	3.486
34	Mtor Signaling Pathway	3.454
35	Oxytocin Signaling Pathway	3.432
36	Pathways In Cancer	3.408
37	Egfr Tyrosine Kinase Inhibitor Resistance	3.406
38	Camp Signaling Pathway	3.338
39	Sphingolipid Signaling Pathway	3.309
40	Proteoglycans In Cancer	3.288
41	Vascular Smooth Muscle Contraction	3.227
42	Rap1 Signaling Pathway	3.208
43	Vibrio Cholerae Infection	3.198
44	Human Cytomegalovirus Infection	2.937
45	Pathogenic Escherichia Coli Infection	2.908
46	Apoptosis	2.871
47	Insulin Signaling Pathway	2.85
48	Apelin Signaling Pathway	2.85
49	Ras Signaling Pathway	2.849
50	Human Papillomavirus Infection	2.83
51	Fluid Shear Stress And Atherosclerosis	2.809
52	Transcriptional Misregulation In Cancer	2.804

53	Prostate Cancer	2.774
54	Glycerophospholipid Metabolism	2.774
55	Endometrial Cancer	2.757
56	Endocrine Resistance	2.745
57	Phospholipase D Signaling Pathway	2.674
58	Melanogenesis	2.664
59	Breast Cancer	2.656
60	C-Type Lectin Receptor Signaling Pathway	2.587
61	Longevity Regulating Pathway - Multiple Species	2.579
62	Regulation Of Actin Cytoskeleton	2.449
63	Tnf Signaling Pathway	2.446
64	Acute Myeloid Leukemia	2.423
65	Butanoate Metabolism	2.402
66	Cgmp-Pkg Signaling Pathway	2.395
67	Epithelial Cell Signaling In Helicobacter Pylori Infection	2.352
68	Prolactin Signaling Pathway	2.284
69	Thermogenesis	2.278
70	Axon Guidance	2.231
71	Melanoma	2.221
72	Cell Cycle	2.17
73	Alcoholism	2.169
74	Endocytosis	2.138
75	Chronic Myeloid Leukemia	2.104
76	Relaxin Signaling Pathway	2.07
77	Chemokine Signaling Pathway	2.066
78	Dopaminergic Synapse	2.054
79	Spliceosome	2.008
80	Epstein-Barr Virus Infection	1.943
81	Peroxisome	1.927
82	ErbB Signaling Pathway	1.881
83	Adrenergic Signaling In Cardiomyocytes	1.868
84	Hepatitis B	1.868
85	Human Immunodeficiency Virus 1 Infection	1.842
86	Gap Junction	1.817
87	Non-Alcoholic Fatty Liver Disease (Nafld)	1.806
88	Gastric Cancer	1.806
89	Mrna Surveillance Pathway	1.757
90	Cushing Syndrome	1.747
91	Hippo Signaling Pathway	1.747
92	Micrnas In Cancer	1.745
93	Gnrh Signaling Pathway	1.72
94	Il-17 Signaling Pathway	1.72
95	Glycine, Serine And Threonine Metabolism	1.682
96	Jak-Stat Signaling Pathway	1.661
97	Bladder Cancer	1.641
98	Nod-Like Receptor Signaling Pathway	1.602
99	Hepatocellular Carcinoma	1.602
100	T Cell Receptor Signaling Pathway	1.583
101	Influenza A	1.573
102	Abc Transporters	1.529
103	Basal Transcription Factors	1.495
104	Pi3K-Akt Signaling Pathway	1.473
105	Kaposi Sarcoma-Associated Herpesvirus Infection	1.447
106	Valine, Leucine And Isoleucine Degradation	1.401
107	Amino Sugar And Nucleotide Sugar Metabolism	1.401

108	Huntington Disease	1.394
109	Cocaine Addiction	1.373
110	Mineral Absorption	1.319
111	Amyotrophic Lateral Sclerosis (Als)	1.319
112	Platelet Activation	1.3
113	Osteoclast Differentiation	1.249
114	Hepatitis C	1.221
115	Natural Killer Cell Mediated Cytotoxicity	1.221
116	Steroid Hormone Biosynthesis	1.14
117	Lysine Degradation	1.14
118	Wnt Signaling Pathway	1.095
119	Arachidonic Acid Metabolism	1.068
120	Cortisol Synthesis And Secretion	1.051
121	Non-Small Cell Lung Cancer	1.019
122	Aminoacyl-Trna Biosynthesis	1.019

Table S5. GO enrichment from LC-MS/MS DEPs

	Gene Ontology Term (GO term)	Enrichment score
1	Retrograde Protein Transport, Er To Cytosol	92.73
2	Positive Regulation Of Glycoprotein Metabolic Process	92.73
3	Vesicle Transport Along Microtubule	49.92
4	Triglyceride Mobilization	46.36
5	Interleukin-8 Secretion	46.36
6	Regulation Of Protein Metabolic Process	30.91
7	Protein C-Linked Glycosylation Via 2'-Alpha-Mannosyl-L-Tryptophan	26.49
8	Growth Hormone Secretion	26.49
9	Leukotriene Biosynthetic Process	18.55
10	Cellular Response To Insulin Stimulus	17.45
11	Virion Assembly	16.86
12	Cargo Loading Into Copii-Coated Vesicle	14.27
13	Positive Regulation Of Ubiquitin Protein Ligase Activity	14.27
14	Establishment Of Endothelial Intestinal Barrier	14.27
15	Er-Associated Misfolded Protein Catabolic Process	14.27
16	Phagocytosis	13.98
17	Lipoprotein Transport	13.25
18	Erad Pathway	13.25
19	Ubiquitin-Dependent Erad Pathway	10.43
20	Regulation Of Actin Cytoskeleton Organization	10.28
21	Rab Protein Signal Transduction	9.71
22	Error-Free Translesion Synthesis	9.27
23	Protein Folding	9.05
24	Melanosome Transport	8.43
25	Proteasome-Mediated Ubiquitin-Dependent Protein Catabolic Process	8.15
26	Intracellular Protein Transport	7.86
27	Neutrophil Degranulation	7.73
28	Receptor-Mediated Endocytosis	7.49
29	Er To Golgi Vesicle-Mediated Transport	7.31
30	Post-Translational Protein Modification	7.27
31	Regulation Of Cell Morphogenesis	7.13
32	Osteoblast Differentiation	6.92
33	Regulation Of Cell Motility	6.62
34	Response To Virus	6.59
35	Protein Methylation	6.18
36	Autophagy	5.92
37	Golgi Organization	5.87
38	Protein Deubiquitination	5.86
39	Atp Metabolic Process	5.8
40	Proteasomal Protein Catabolic Process	5.45
41	Actin Cytoskeleton Organization	4.79
42	Substrate Adhesion-Dependent Cell Spreading	4.52
43	Response To Lipopolysaccharide	4.29
44	Biological_Process	4.01
45	Translation	3.7
46	Autophagosome Assembly	3.37
47	Retinoid Metabolic Process	3.25
48	Negative Regulation Of Neuron Projection Development	3.25
49	Cerebral Cortex Development	3.14
50	Antimicrobial Humoral Immune Response Mediated By Antimicrobial Peptide	3.09
51	Copii Vesicle Coating	2.94

52	Positive Regulation Of Protein Catabolic Process	2.51
53	Response To Endoplasmic Reticulum Stress	2.51
54	Lipid Catabolic Process	2.23
55	Rho Protein Signal Transduction	2.23
56	Retrograde Vesicle-Mediated Transport, Golgi To Er	2.21
57	Actin Filament Organization	1.77
58	Vesicle-Mediated Transport	1.57
59	Cellular Response To Tumor Necrosis Factor	1.52
60	Platelet Degranulation	1.5
61	Protein Phosphorylation	1.48
62	Negative Regulation Of Neuron Apoptotic Process	1.43
63	Positive Regulation Of Cell Proliferation	1.4
64	Lipid Metabolic Process	1.38
65	Oxidation-Reduction Process	1.27
66	Endocytosis	1.25
67	Aging	1.17
68	Cytoskeleton Organization	1.14

Table S6. KEGG enrichment from LC-MS/MS DEPs

	KEGG pathway	Enrichment score
1	Protein Processing In Endoplasmic Reticulum	7.805
2	Legionellosis	7.178
3	Vitamin Digestion And Absorption	6.919
4	Fat Digestion And Absorption	4.05
5	Proteasome	3.69
6	Ether Lipid Metabolism	3.533
7	Amino Sugar And Nucleotide Sugar Metabolism	3.46
8	Cholesterol Metabolism	3.321
9	Phagosome	2.597
10	Aminoacyl-Trna Biosynthesis	2.516
11	Metabolic Pathways	2.444
12	Ppar Signaling Pathway	2.244
13	Amoebiasis	1.73
14	Glycerophospholipid Metabolism	1.712
15	Insulin Resistance	1.552
16	Vascular Smooth Muscle Contraction	1.372
17	Systemic Lupus Erythematosus	1.249
18	Spliceosome	1.239

Table S7. List of qPCR primers

Species	Gene	Forward primer (5'-3')	Reverse primer (5'-3')
<i>D. rerio</i>	<i>atg10l</i>	TCAC TTTCGTGCGAGTGTCT	CACTCGTCTGAAAAGGGCCA
	<i>bnip4</i>	CAGTCCCAGACGTGTCCAGA	GATCCTTGCAACAGCTTCGG
	<i>fabp10a</i>	AACTCCTTCACCATCGGCAA	ATCATGGTGGTTCCTCCGAC
	<i>fdps</i>	TGAGCCAGGACGAGTCCATA	CCTCCAGGGGCATTGTACTG
	<i>lsm12b</i>	CGTCGTAATCTCACCACCGT	TCCTTCTGTGTTTGCTGTGC
	<i>lss</i>	GGCATT TGCGTGTATGGGTC	ATCAATCCCAGCAAAGCCCA
	<i>map1lc3a</i>	ACCCTTCAAACAACGACGGA	TGGAAGTTGCTTTTCCCCCT
	<i>mvk</i>	GAGCATTCTGTCGTGCATGG	AAGTTCCTTGGGGTCCCTCT
	<i>rpl13a</i>	ATCATGGCGGACCGATTCAA	TCTTGCGGAGGAAAGCCAAA
<i>H. sapiens</i>	<i>ACTB</i>	ACCATGGATGATGATATCGC	CATAGGAATCCTTCTGACCCA
	<i>FDPS</i>	GGTAGTAGCATTCCGGGAG	ATTGATGGCATCCAAACCCA
	<i>HMGCR</i>	TAGCTGGACGCAACCTTTAT	TAGCAGCAGGTTTCTTGTC
	<i>HMGCS</i>	ACCGCTGCTATTCTGTCTAC	GTCATT CAGCAACATCCGAG
	<i>LSS</i>	GAGCGGCGTTATTTGCAGAG	AGACACCGGACTCCTCTCTC
	<i>MVK</i>	TTCCCAGGAGCCATGTTGTC	TACAGCCAGTGCTACCTTGC
	<i>TBP</i>	GTTCAGCAGTCAACGTCCCA	TCATGGGGGAGGGATACAGT

Adjusted weighted average of gene expression within KEGG pathway nodes

The weighted single gene is calculated taking the relative expression level of a gene (Z:A, log₂) and multiplying it by the complement of the statistical significance of the relative expression (1 - p-value). Using this method, gene with a less statistically significant difference has a higher p-value which when complemented will be closer to zero and when multiplied by the gene expression level will result in a lower magnitude weighted gene expression. A gene with more statistically significant difference has a lower p-value which when complemented will be closer to one, which will result in less changed magnitude weighted gene expression. Overall, this will decrease the perceived influence of less significant genes whereas more significant genes remain more unchanged. A weighting power is applied to increase the weighting given to the statistical significance.

$$\text{Weighted single gene} = \text{gene expression} \times (1 - \text{significance})^{\text{weight}}$$

Example (weight of 5):

Gene	Expression (Z:A, Log2)	Significance (Z:A, p-value)	Weighted single gene (Z:A)
<i>lmnb1</i>	-0.60	0.27	-0.12
<i>lmna</i>	-0.90	0.00	-0.89
<i>lmnb2</i>	0.20	0.87	0.00

In signalling pathway networks, individual nodes often contain multiple genes that contribute to the node as each gene performs the function of the node. The one-to-many relationship of human to zebrafish orthologs exacerbates the number of genes in nodes. To apply the weighting methodology to multiple genes within a node, a weighted averaged is calculated. The weighted single gene expressions are summed and divided by the sum of the significance to calculate the weighted multiple gene.

$$\text{Weighted multiple gene} = \frac{\sum_{\text{node genes}} (\text{gene expression} \times (1 - \text{significance})^{\text{weight}})}{\sum_{\text{node genes}} ((1 - \text{significance})^{\text{weight}})}$$

One limitation of a weighted average is nodes where all genes have little significance can be misleading as the denominator remains small, so the weighting on significance is lost. This is adjusted for by multiplying the weighted multiple gene by the complement of the product of all the genes' significance - that is the overall significance of the node. Again, this significance is given a weighting power.

$$\text{Adjusted weighted multiple gene} = \frac{\sum_{\text{node genes}} (\text{gene expression} \times (1 - \text{significance})^{\text{weight}})}{\sum_{\text{node genes}} ((1 - \text{significance})^{\text{weight}})} \times (1 - \prod_{\text{node genes}} \text{significance})^{\text{weight}}$$