

Supplementary Figures and Tables

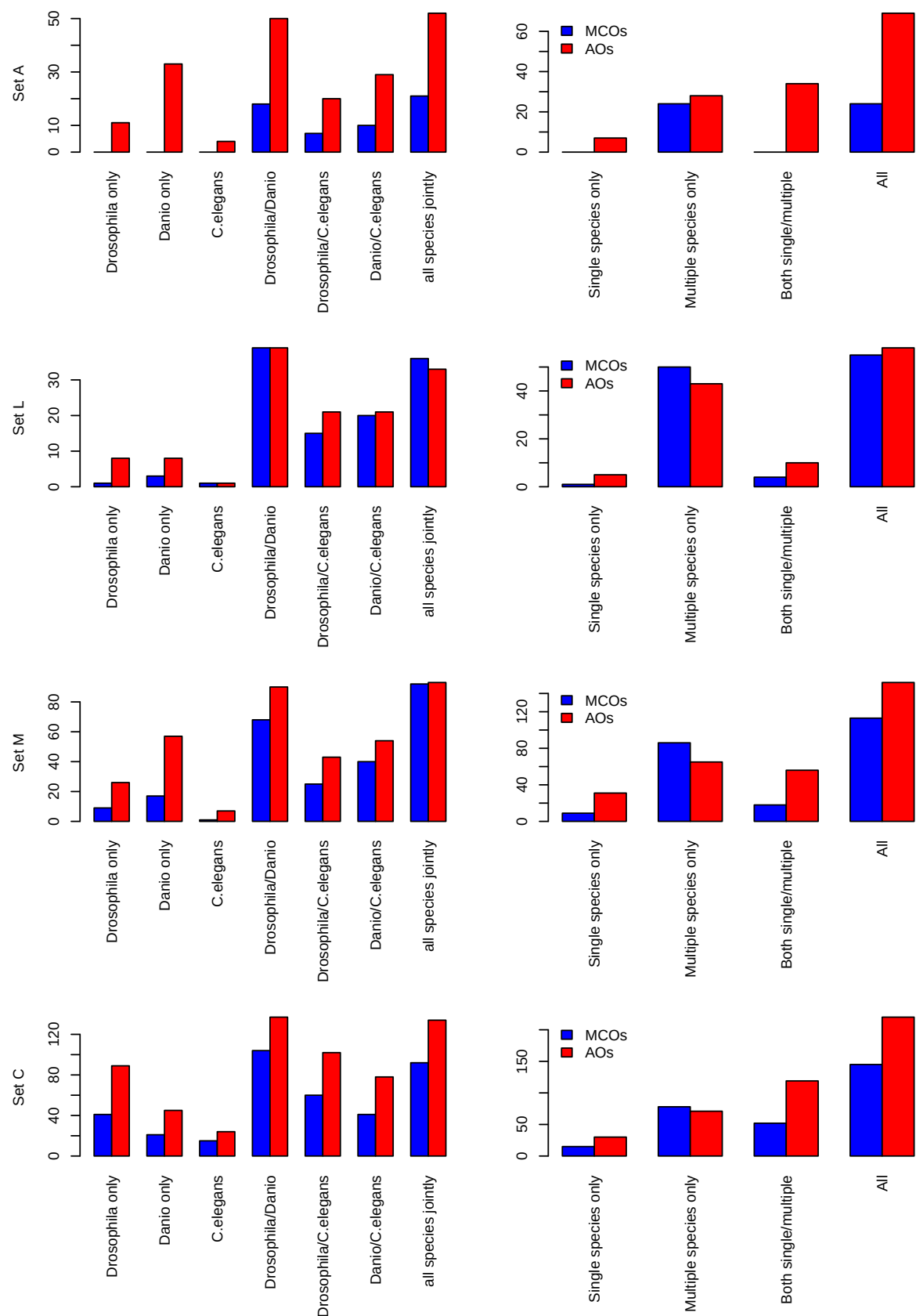


Figure S1. Supplementary Figure related to Figure 4. MSGEA vs. single species enrichment analysis for clusters of orthologous proteins (COPs). Number of significant terms shown for each of the four sets *A*, *L*, *M*, and *C* (cf. Figure 1).

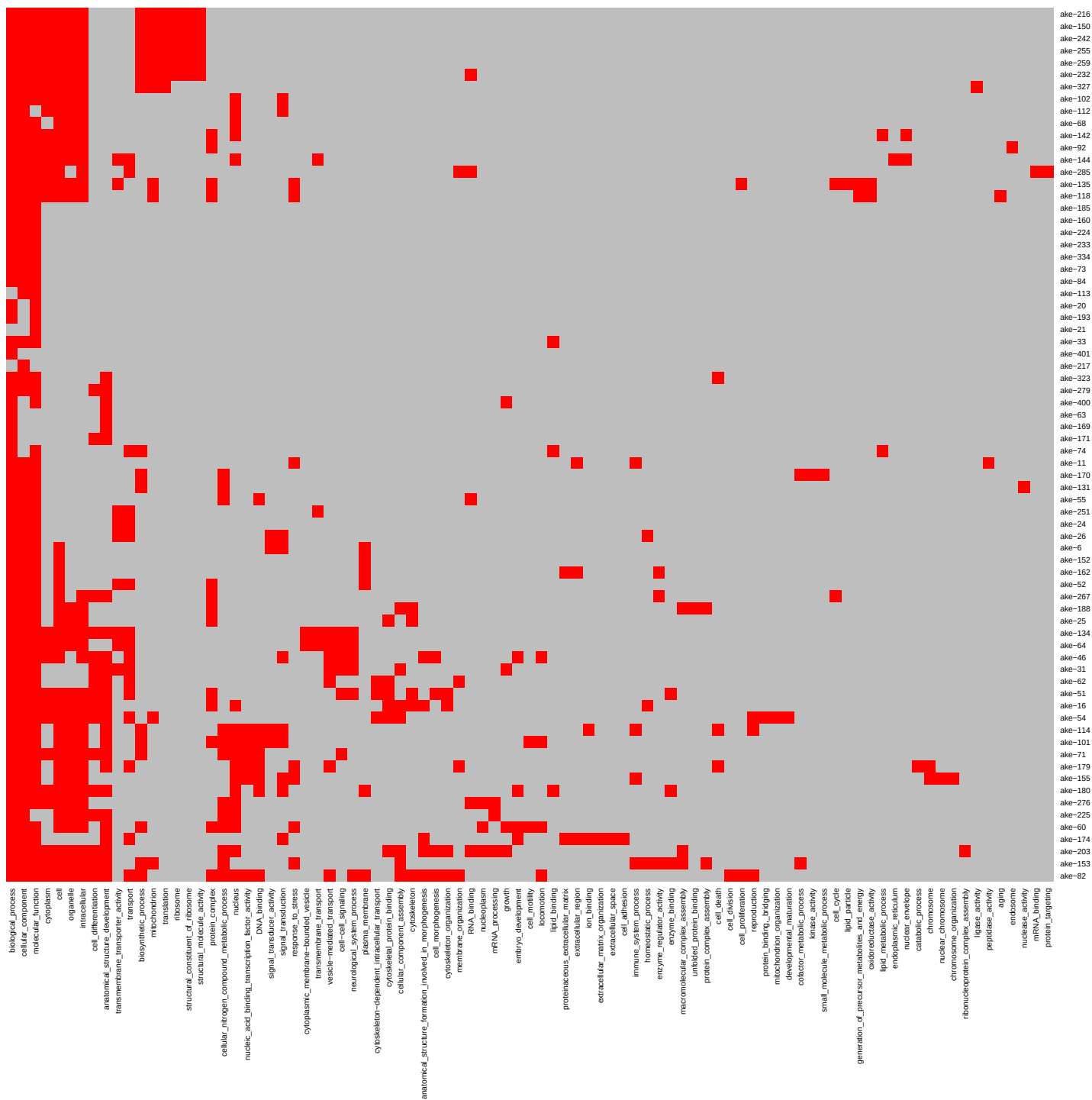


Figure S2. Supplementary Figure related to Figure 5. Absence/presence map of GO-slim terms. *x*-axis: GO-slim terms (including all GO levels); right *y*-axis: internal COP IDs.

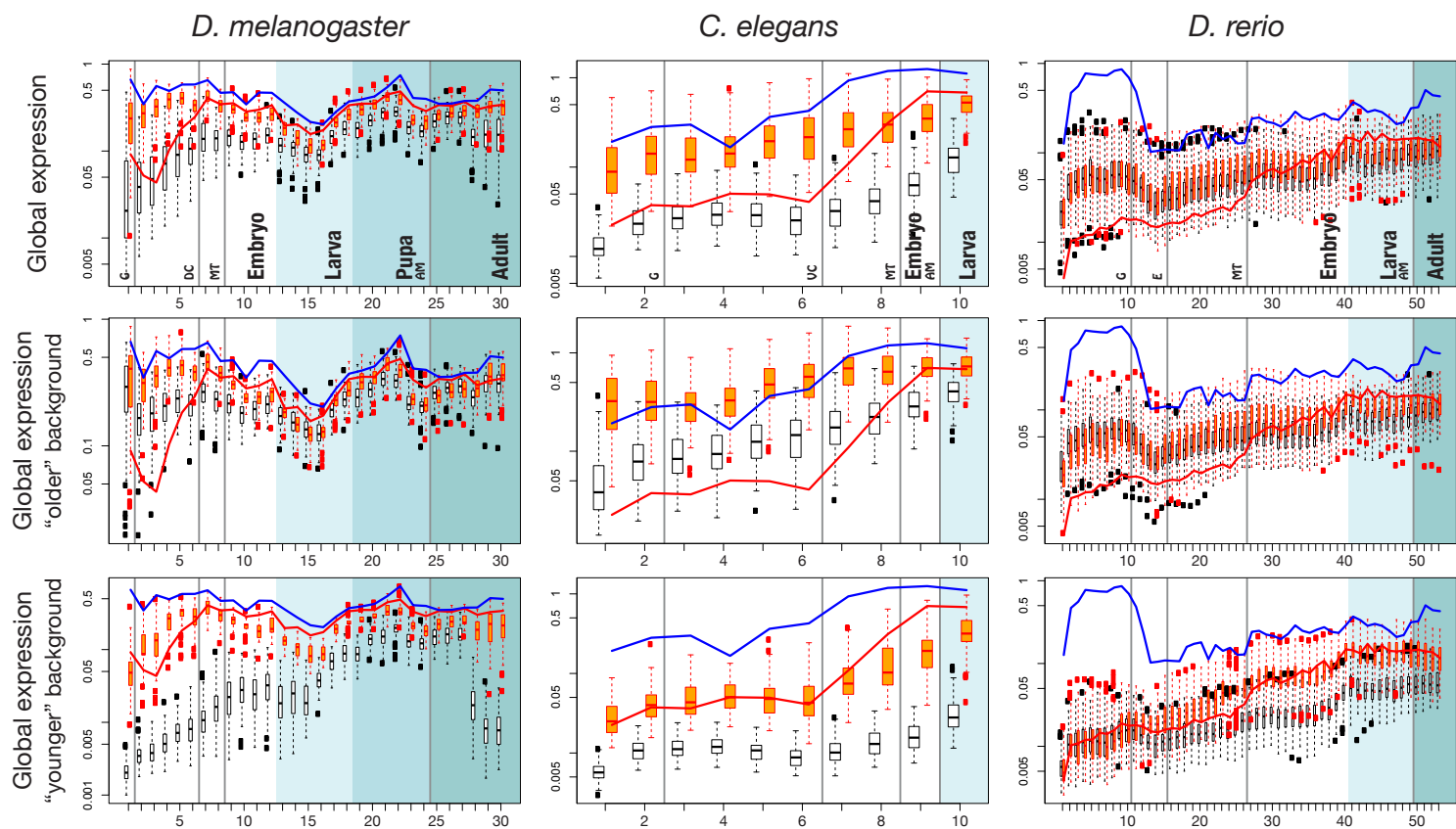


Figure S3. Supplementary Figure related to Figure 3. Expression profiles with background distribution based on medians, instead of means. Color code and other labels as in Figure 5.

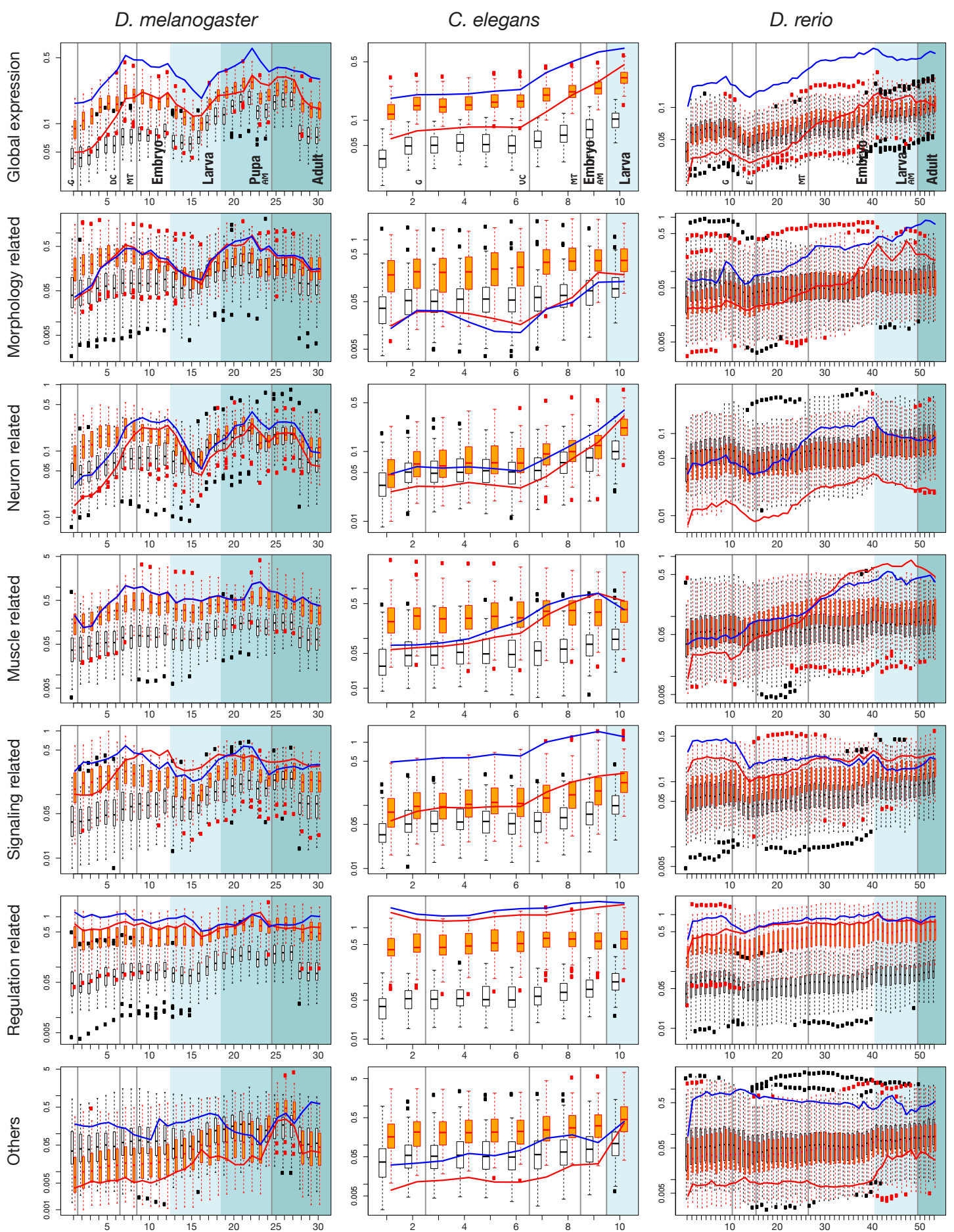


Figure S4. Supplementary Figure related to Figure 3. Expression profiles of set L' genes by functional classes. Background distributions based on mean expression values. Color code and other labels as in Figure 5. *D.m.*, 'muscle': there are no paralogs; therefore, only the blue line (for MCOs) is displayed.

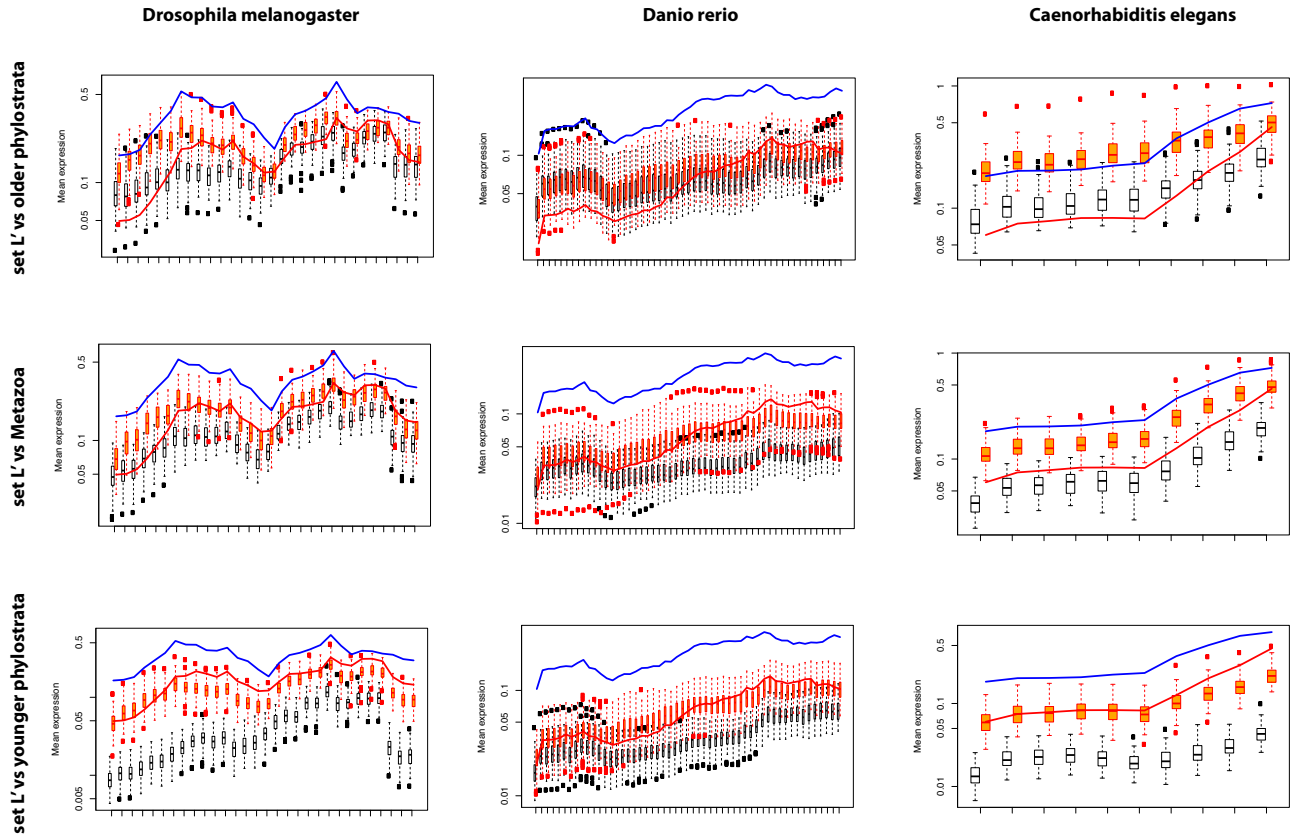


Figure S5. Supplementary Figure related to Figure 3. Expression profiles of set L' genes compared to different background distributions, including all phylostratigraphically older and younger genes at the top and bottom, and all Metazoan genes in the middle. Background distributions based on mean expression values. Color code and other labels as in Figure 5.

Table S1. Supplementary Table related to Figure 1. Distribution of losses in set *L*.

number of clusters	species affected	lineage affected
[33]	[APL]	[APL only]
31	APL*, CEL	CEL only
22	APL*, STR	STR only
8	APL*, HEL	HEL only
6	APL*, ANO, DRO	insects
6	APL*, ANO	ANO only
4	APL*, MUS	MUS only
4	APL*, LOT	LOT only
4	APL*, CAP	CAP only
3	APL*, DRO	DRO only
2	APL*, HEL, CAP	annelids
1	ANO	ANO only
1	-	-

*due to the incomplete assembly and annotation status of the *A. californica* genome, APL was ignored when determining the number of losses. When *A. californica* is included only one cluster contains orthologs from all species (last line). Omitting *A. californica*, we find 33 clusters which contain orthologs from nine species (first line). In the remaining 91 clusters in set *L* an ortholog from at least one species is missing. Most losses (31 of 91) are *C. elegans*-specific (second line).

Table S2. Supplementary Table with annotation of x -axis tick marks in Figure 5, Figure S3 and Figure S4 according to [75] (*D. melanogaster*), [124] (*C. elegans*) and [48] (*D. rerio*).

bckgr-color	tickmark	devel. stage	bckgr-color	tickmark	devel. stage
<i>D. rerio</i>			<i>D. melanogaster</i>		
white	1	egg 0min	white	1	embryos 0-2hr
	2	zygote 15min		2	embryos 2-4hr
	3	cleavage 45min		3	embryos 4-6hr
	4	cleavage 1h15min		4	embryos 6-8hr
	5	cleavage 1h45min		5	embryos 8-10hr
	6	blastula 2h15min		6	embryos 10-12hr
	7	blastula 2h45min		7	embryos 12-14hr
	8	blastula 3h20min		8	embryos 14-16hr
	9	blastula 4h		9	embryos 16-18hr
	10	blastula 4h40min		10	embryos 18-20hr
	11	gastrula 5h20min		11	embryos 20-22hr
	12	gastrula 6h		12	embryos 22-24hr
	13	gastrula 7h	light grey	13	L1 larvae
	14	gastrula 8h		14	L2 larvae
	15	gastrula 9h		15	L3 larvae 12hr post molt
	16	gastrula 10h	grey	16	L3 larvaePS 1-2
	17	segmentation 10h20min		17	L3 larvaePS 3-6
	18	segmentation 11h		18	L3 larvaePS 7-9
	19	segmentation 11h40min		19	white prepupae
	20	segmentation 12h		20	WPP 12hr
	21	segmentation 13h		21	WPP 24hr
	22	segmentation 14h		22	pupae WPP 2d
	23	segmentation 15h		23	pupae WPP 3d
	24	segmentation 16h		24	pupae WPP 4d
	25	segmentation 17h	dark grey	25	adult male 1d
	26	segmentation 18h		26	adult male 30d
	27	segmentation 19h		27	adult male 5d
	28	segmentation 20h		28	adult female 1d
	29	segmentation 21h		29	adult female 5d
	30	segmentation 22h		30	adult female 30d
	31	segmentation 23h			
	32	pharyngula 1d1h			
	33	pharyngula 1d3h			
	34	pharyngula 1d6h			
	35	pharyngula 1d10h			
	36	pharyngula 1d14h			
	37	pharyngula 1d18h			
	38	hatching 2d			
	39	hatching 2d12h			
	40	hatching 3d			
light grey	41	larva 4d	white	1	stage1
	42	larva 6d		2	stage2
	43	larva 8d		3	stage3
	44	larva 10d		4	stage4
	45	larva 14d		5	stage5
	46	larva 18d		6	stage6
	47	larva 24d		7	stage7
	48	larva 30d		8	stage8
	49	larva 40d		9	stage9
dark grey	50	juvenile 45d	light grey	10	stage10
	51	juvenile 55d			
	52	juvenile 65d			
	53	juvenile 80d			

Table S3. Supplementary Table related to Figure S3 and Figure S4. Comparison of developmental stages among *Drosophila*, *Caenorhabditis*, and *Danio*

[illegible]

Table S4. Supplementary Table related to Figures 4 and 5. GO terms (of level ≥ 4) identified in 85 COPs of set L' . COPs ake-68, ake-73, ake-185, ake-217 and ake-224 did not contain GO terms of level ≥ 4 and do therefore not occur in this table.

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0000122	regulation	negative regulation of transcription from RNA polymerase II promoter	114, 37, 82
GO:0000188	signalling	inactivation of MAPK activity	3
GO:0000226	muscle	microtubule cytoskeleton organization	120, 51
GO:0000278	morphology	mitotic cell cycle	135, 267
GO:0000280	signalling	nuclear division	16
GO:0000302	signalling	response to reactive oxygen species	118
GO:0000381	regulation	regulation of alternative nuclear mRNA splicing, via spliceosome	276
GO:0000387	signalling	spliceosomal snRNP assembly	203
GO:0000422	regulation	mitochondrion degradation	193
GO:0001525	morphology	angiogenesis	6
GO:0001653	signalling	peptide receptor activity	6
GO:0001666	signalling	response to hypoxia	135, 193
GO:0001708	morphology	cell fate specification	82
GO:0001709	morphology	cell fate determination	32
GO:0001751	neuron	compound eye photoreceptor cell differentiation	180, 32
GO:0001754	neuron	eye photoreceptor cell differentiation	64, 82
GO:0001756	morphology	somitogenesis	2, 37, 6
GO:0001946	morphology	lymphangiogenesis	82
GO:0001947	muscle	heart looping	3
GO:0001964	signalling	startle response	37, 55
GO:0002009	morphology	morphogenesis of an epithelium	120, 16, 171, 92
GO:0002074	muscle	extraocular skeletal muscle development	71
GO:0002119	morphology	nematode larval development	114, 131, 150, 155, 16, 171, 174, 180, 18, 203, 216, 232, 242, 255, 259, 279, 46, 71, 82, 92, 97
GO:0002121	signalling	inter-male aggressive behavior	52, 55
GO:0002385	signalling	mucosal immune response	155
GO:0003140	morphology	determination of left/right asymmetry in lateral mesoderm	3
GO:0003146	muscle	heart jogging	3
GO:0003707	signalling	steroid hormone receptor activity	114
GO:0003810	signalling	protein-glutamine gamma-glutamyltransferase activity	3
GO:0003917	regulation	DNA topoisomerase type I activity	3
GO:0003918	regulation	DNA topoisomerase (ATP-hydrolyzing) activity	3
GO:0003924	signalling	GTPase activity	3
GO:0003951	regulation	NAD ⁺ kinase activity	170
GO:0003954	regulation	NADH dehydrogenase activity	118
GO:0004091	signalling	carboxylesterase activity	51
GO:0004129	signalling	cytochrome-c oxidase activity	135
GO:0004190	signalling	aspartic-type endopeptidase activity	113
GO:0004221	signalling	ubiquitin thiolesterase activity	3
GO:0004252	signalling	serine-type endopeptidase activity	11
GO:0004308	signalling	exo-alpha-sialidase activity	3
GO:0004386	signalling	helicase activity	162
GO:0004518	signalling	nuclease activity	131
GO:0004519	signalling	endonuclease activity	131
GO:0004521	signalling	endoribonuclease activity	131
GO:0004553	signalling	hydrolase activity, hydrolyzing O-glycosyl compounds	51
GO:0004556	signalling	alpha-amylase activity	27
GO:0004672	signalling	protein kinase activity	144
GO:0004674	signalling	protein serine/threonine kinase activity	144
GO:0004725	signalling	protein tyrosine phosphatase activity	3
GO:0004812	regulation	aminoacyl-tRNA ligase activity	160, 32
GO:0004842	signalling	ubiquitin-protein ligase activity	2

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0004887	signalling	thyroid hormone receptor activity	114
GO:0004888	signalling	transmembrane signaling receptor activity	6
GO:0004930	signalling	G-protein coupled receptor activity	3, 6
GO:0004948	signalling	calcitonin receptor activity	6
GO:0004991	signalling	parathyroid hormone receptor activity	6
GO:0005085	signalling	guanyl-nucleotide exchange factor activity	63
GO:0005086	signalling	ARF guanyl-nucleotide exchange factor activity	3
GO:0005089	signalling	Rho guanyl-nucleotide exchange factor activity	63
GO:0005184	neuron	neuropeptide hormone activity	6
GO:0005216	signalling	ion channel activity	144, 3, 52
GO:0005253	signalling	anion channel activity	19
GO:0005254	signalling	chloride channel activity	19, 52
GO:0005261	signalling	cation channel activity	144
GO:0005262	signalling	calcium channel activity	134
GO:0005267	signalling	potassium channel activity	144
GO:0005277	signalling	acetylcholine transmembrane transporter activity	251
GO:0005278	signalling	acetylcholine:hydrogen antiporter activity	251
GO:0005326	neuron	neurotransmitter transporter activity	31
GO:0005430	neuron	synaptic vesicle amine transmembrane transporter activity	64
GO:0005786	signalling	signal recognition particle, endoplasmic reticulum targeting	285
GO:0005802	signalling	trans-Golgi network	18
GO:0005913	signalling	cell-cell adherens junction	180
GO:0005975	signalling	carbohydrate metabolic process	27, 51
GO:0006030	morphology	chitin metabolic process	2
GO:0006120	regulation	mitochondrial electron transport, NADH to ubiquinone	118
GO:0006123	regulation	mitochondrial electron transport, cytochrome c to oxygen	135
GO:0006171	signalling	cAMP biosynthetic process	6
GO:0006184	signalling	GTP catabolic process	3
GO:0006200	regulation	ATP catabolic process	162, 3
GO:0006260	regulation	DNA replication	3
GO:0006265	regulation	DNA topological change	3
GO:0006281	regulation	DNA repair	33
GO:0006306	regulation	DNA methylation	6
GO:0006351	regulation	transcription, DNA-dependent	101, 2, 3, 37, 71
GO:0006355	regulation	regulation of transcription, DNA-dependent	101, 114, 2, 32, 37, 3, 71, 82
GO:0006357	regulation	regulation of transcription from RNA polymerase II promoter	101, 37
GO:0006364	regulation	rRNA processing	401
GO:0006396	regulation	RNA processing	225
GO:0006397	signalling	mRNA processing	203, 276
GO:0006412	regulation	translation	150, 216, 232, 242, 255, 259, 327, 97
GO:0006418	regulation	tRNA aminoacylation for protein translation	160, 32
GO:0006450	regulation	regulation of translational fidelity	327
GO:0006457	signalling	protein folding	112
GO:0006468	signalling	protein phosphorylation	144
GO:0006470	signalling	protein dephosphorylation	3
GO:0006486	signalling	protein glycosylation	2, 3
GO:0006508	signalling	proteolysis	113, 3
GO:0006511	signalling	ubiquitin-dependent protein catabolic process	3
GO:0006614	regulation	SRP-dependent cotranslational protein targeting to membrane	285
GO:0006629	signalling	lipid metabolic process	142
GO:0006694	signalling	steroid biosynthetic process	74
GO:0006754	regulation	ATP biosynthetic process	3
GO:0006811	signalling	ion transport	144, 3, 52
GO:0006812	signalling	cation transport	3

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0006813	signalling	potassium ion transport	144, 26
GO:0006814	signalling	sodium ion transport	24, 3
GO:0006820	signalling	anion transport	19
GO:0006821	signalling	chloride transport	19, 52
GO:0006826	signalling	iron ion transport	3
GO:0006836	neuron	neurotransmitter transport	101, 251, 31, 64
GO:0006855	signalling	drug transmembrane transport	251, 64
GO:0006869	signalling	lipid transport	74
GO:0006874	signalling	cellular calcium ion homeostasis	5
GO:0006879	signalling	cellular iron ion homeostasis	3
GO:0006884	signalling	cell volume homeostasis	19
GO:0006885	signalling	regulation of pH	3
GO:0006886	signalling	intracellular protein transport	14
GO:0006898	signalling	receptor-mediated endocytosis	102, 120, 131, 150, 232, 242, 259, 279, 46, 92
GO:0006911	signalling	phagocytosis, engulfment	52, 62, 82
GO:0006914	signalling	autophagy	193
GO:0006915	signalling	apoptotic process	3
GO:0006952	signalling	defense response	152, 2
GO:0007005	regulation	mitochondrion organization	5
GO:0007015	neuron	actin filament organization	120
GO:0007021	muscle	tubulin complex assembly	188
GO:0007026	muscle	negative regulation of microtubule depolymerization	25
GO:0007030	signalling	Golgi organization	135
GO:0007165	signalling	signal transduction	101, 112, 174, 180, 2, 3, 6
GO:0007166	signalling	cell surface receptor signaling pathway	6
GO:0007173	signalling	epidermal growth factor receptor signaling pathway	37
GO:0007186	signalling	G-protein coupled receptor signaling pathway	3, 6
GO:0007218	neuron	neuropeptide signaling pathway	6
GO:0007219	signalling	Notch signaling pathway	37, 46
GO:0007265	signalling	Ras protein signal transduction	180
GO:0007276	signalling	gamete generation	171
GO:0007281	morphology	germ cell development	276
GO:0007287	signalling	Nebenkern assembly	54
GO:0007297	signalling	ovarian follicle cell migration	32
GO:0007304	morphology	chorion-containing eggshell formation	32
GO:0007349	signalling	cellularization	46
GO:0007368	morphology	determination of left/right symmetry	3
GO:0007391	morphology	dorsal closure	46
GO:0007398	morphology	ectoderm development	37
GO:0007399	neuron	nervous system development	16, 37, 46, 51, 82
GO:0007400	neuron	neuroblast fate determination	82
GO:0007402	neuron	ganglion mother cell fate determination	82
GO:0007405	neuron	neuroblast proliferation	82
GO:0007406	neuron	negative regulation of neuroblast proliferation	82
GO:0007409	neuron	axonogenesis	16, 203, 51, 82
GO:0007411	neuron	axon guidance	82
GO:0007416	neuron	synapse assembly	82
GO:0007417	neuron	central nervous system development	82
GO:0007419	neuron	ventral cord development	174, 82
GO:0007420	neuron	brain development	3, 82
GO:0007422	neuron	peripheral nervous system development	32, 37, 82
GO:0007423	morphology	sensory organ development	82
GO:0007424	morphology	open tracheal system development	101
GO:0007426	morphology	tracheal outgrowth, open tracheal system	180
GO:0007427	signalling	epithelial cell migration, open tracheal system	101
GO:0007443	morphology	Malpighian tubule morphogenesis	174
GO:0007465	neuron	R7 cell fate commitment	82
GO:0007476	morphology	imaginal disc-derived wing morphogenesis	180
GO:0007498	morphology	mesoderm development	174, 37, 5

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0007507	muscle	heart development	16, 2, 60
GO:0007517	muscle	muscle organ development	16, 71
GO:0007519	muscle	skeletal muscle tissue development	16, 71
GO:0007527	muscle	adult somatic muscle development	169
GO:0007528	neuron	neuromuscular junction development	203, 51
GO:0007552	morphology	metamorphosis	114
GO:0007553	morphology	regulation of ecdysteroid metabolic process	114
GO:0007591	morphology	molting cycle, chitin-based cuticle	114
GO:0007606	signalling	sensory perception of chemical stimulus	3
GO:0007616	neuron	long-term memory	22
GO:0007619	signalling	courtship behavior	82
GO:0008026	regulation	ATP-dependent helicase activity	162
GO:0008036	signalling	diuretic hormone receptor activity	6
GO:0008045	neuron	motor axon guidance	46
GO:0008049	signalling	male courtship behavior	6
GO:0008081	signalling	phosphoric diester hydrolase activity	33
GO:0008083	signalling	growth factor activity	3
GO:0008088	neuron	axon cargo transport	51, 62
GO:0008101	signalling	decapentaplegic signaling pathway	32
GO:0008104	signalling	protein localization	82
GO:0008137	regulation	NADH dehydrogenase (ubiquinone) activity	118
GO:0008138	signalling	protein tyrosine/serine/threonine phosphatase activity	3
GO:0008168	signalling	methyltransferase activity	6
GO:0008188	neuron	neuropeptide receptor activity	6
GO:0008233	signalling	peptidase activity	3
GO:0008234	signalling	cysteine-type peptidase activity	3
GO:0008284	signalling	positive regulation of cell proliferation	32
GO:0008285	signalling	negative regulation of cell proliferation	82
GO:0008293	signalling	torso signaling pathway	180
GO:0008355	neuron	olfactory learning	51
GO:0008356	morphology	asymmetric cell division	82
GO:0008373	signalling	sialyltransferase activity	3
GO:0008380	regulation	RNA splicing	203, 276
GO:0008417	signalling	fucosyltransferase activity	2
GO:0008504	signalling	monoamine transmembrane transporter activity	64
GO:0008508	signalling	bile acid:sodium symporter activity	24
GO:0008582	neuron	regulation of synaptic growth at neuromuscular junction	51
GO:0008587	morphology	imaginal disc-derived wing margin morphogenesis	37
GO:0008595	morphology	anterior/posterior axis specification, embryo	180
GO:0008898	signalling	homocysteine S-methyltransferase activity	2
GO:0009303	regulation	rRNA transcription	131
GO:0009306	signalling	protein secretion	46
GO:0009651	signalling	response to salt stress	155
GO:0009792	morphology	embryo development ending in birth or egg hatching	118, 131, 150, 155, 16, 169, 174, 193, 203, 21, 216, 232, 242, 255, 259, 276, 323, 334, 46, 51, 71, 92, 97
GO:0009881	signalling	photoreceptor activity	26
GO:0009966	signalling	regulation of signal transduction	180
GO:0009996	morphology	negative regulation of cell fate specification	32
GO:0010001	neuron	glial cell differentiation	82
GO:0010171	morphology	body morphogenesis	114, 120, 16, 18, 71
GO:0010466	signalling	negative regulation of peptidase activity	162
GO:0010468	signalling	regulation of gene expression	401
GO:0010629	signalling	negative regulation of gene expression	112, 37
GO:0010866	signalling	regulation of triglyceride biosynthetic process	155
GO:0010867	signalling	positive regulation of triglyceride biosynthetic process	142
GO:0014036	neuron	neural crest cell fate specification	3

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0014812	muscle	muscle cell migration	60
GO:0015077	signalling	monovalent inorganic cation transmembrane transporter activity	3
GO:0015143	signalling	urate transmembrane transporter activity	21
GO:0015238	signalling	drug transmembrane transporter activity	251, 64
GO:0015269	signalling	calcium-activated potassium channel activity	26
GO:0015297	signalling	antiporter activity	3
GO:0015299	signalling	solute:hydrogen antiporter activity	3
GO:0015385	signalling	sodium:hydrogen antiporter activity	3
GO:0015662	regulation	ATPase activity, coupled to transmembrane movement of ions, phosphorylative mechanism	3
GO:0015672	signalling	monovalent inorganic cation transport	144, 3
GO:0015721	signalling	bile acid and bile salt transport	24
GO:0015842	neuron	synaptic vesicle amine transport	64
GO:0015844	signalling	monoamine transport	64
GO:0015872	signalling	dopamine transport	64
GO:0015893	signalling	drug transport	251, 64
GO:0015934	signalling	large ribosomal subunit	232
GO:0015992	signalling	proton transport	135, 3
GO:0016057	neuron	regulation of membrane potential in photoreceptor cell	26
GO:0016070	regulation	RNA metabolic process	55
GO:0016079	neuron	synaptic vesicle exocytosis	31
GO:0016202	muscle	regulation of striated muscle tissue development	71
GO:0016286	signalling	small conductance calcium-activated potassium channel activity	26
GO:0016301	signalling	kinase activity	144, 26
GO:0016307	signalling	phosphatidylinositol phosphate kinase activity	14, 2
GO:0016310	signalling	phosphorylation	144, 170, 26
GO:0016311	signalling	dephosphorylation	3
GO:0016319	neuron	mushroom body development	114, 52
GO:0016337	signalling	cell-cell adhesion	3
GO:0016360	morphology	sensory organ precursor cell fate determination	37
GO:0016477	morphology	cell migration	46
GO:0016567	signalling	protein ubiquitination	2
GO:0016568	morphology	chromatin modification	3
GO:0016746	signalling	transferase activity, transferring acyl groups	251
GO:0016757	signalling	transferase activity, transferring glycosyl groups	2, 3
GO:0016772	signalling	transferase activity, transferring phosphorus-containing groups	144
GO:0016791	signalling	phosphatase activity	3
GO:0016798	signalling	hydrolase activity, acting on glycosyl bonds	27
GO:0016820	signalling	hydrolase activity, acting on acid anhydrides, catalyzing transmembrane movement of substances	3
GO:0016887	regulation	ATPase activity	3
GO:0017017	signalling	MAP kinase tyrosine/serine/threonine phosphatase activity	3
GO:0017053	signalling	transcriptional repressor complex	37
GO:0017127	signalling	cholesterol transporter activity	74
GO:0018149	signalling	peptide cross-linking	3
GO:0018990	morphology	ecdysis, chitin-based cuticle	114
GO:0018996	morphology	molting cycle, collagen and cuticulin-based cuticle	114, 131, 46, 82, 92
GO:0019730	signalling	antimicrobial humoral response	114
GO:0019888	signalling	protein phosphatase regulator activity	267
GO:0019895	regulation	kinesin-associated mitochondrial adaptor activity	54
GO:0019896	neuron	axon transport of mitochondrion	54
GO:0019915	signalling	lipid storage	179, 19, 20, 22, 51, 5, 74
GO:0021884	neuron	forebrain neuron development	82
GO:0021905	neuron	forebrain-midbrain boundary formation	3
GO:0022008	neuron	neurogenesis	171, 267, 279, 46, 62
GO:0030001	signalling	metal ion transport	18
GO:0030097	signalling	hemopoiesis	18

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0030111	signalling	regulation of Wnt receptor signaling pathway	400, 60
GO:0030154	morphology	cell differentiation	71
GO:0030163	signalling	protein catabolic process	92
GO:0030239	muscle	myofibril assembly	16, 5, 82
GO:0030240	muscle	skeletal muscle thin filament assembly	203, 5
GO:0030289	signalling	protein phosphatase 4 complex	267
GO:0030301	signalling	cholesterol transport	74
GO:0030307	signalling	positive regulation of cell growth	32
GO:0030382	regulation	sperm mitochondrion organization	54
GO:0030414	signalling	peptidase inhibitor activity	162
GO:0030421	signalling	defecation	16
GO:0030707	signalling	ovarian follicle cell development	32
GO:0030916	signalling	otic vesicle formation	174
GO:0031016	morphology	pancreas development	60
GO:0031453	signalling	positive regulation of heterochromatin assembly	155
GO:0031618	signalling	nuclear centromeric heterochromatin	155
GO:0032012	signalling	regulation of ARF protein signal transduction	3
GO:0032474	morphology	otolith morphogenesis	174
GO:0034220	signalling	ion transmembrane transport	135, 3, 52
GO:0034605	signalling	cellular response to heat	155
GO:0034707	signalling	chloride channel complex	52
GO:0035023	signalling	regulation of Rho protein signal transduction	63
GO:0035050	morphology	embryonic heart tube development	3
GO:0035071	signalling	salivary gland cell autophagic cell death	323, 32
GO:0035072	signalling	ecdysone-mediated induction of salivary gland cell autophagic cell death	114
GO:0035098	signalling	ESC/E(Z) complex	3
GO:0035147	signalling	branch fusion, open tracheal system	101
GO:0035188	morphology	hatching	267
GO:0035199	signalling	salt aversion	3
GO:0035238	signalling	vitamin A biosynthetic process	64
GO:0035282	morphology	segmentation	32
GO:0035304	signalling	regulation of protein dephosphorylation	267
GO:0035307	signalling	positive regulation of protein dephosphorylation	142
GO:0035335	signalling	peptidyl-tyrosine dephosphorylation	3
GO:0035462	morphology	determination of left/right asymmetry in dien-cephalon	3
GO:0035469	morphology	determination of pancreatic left/right asymmetry	3
GO:0035556	signalling	intracellular signal transduction	184, 63
GO:0036065	signalling	fucosylation	2
GO:0040002	morphology	collagen and cuticulin-based cuticle development	18
GO:0040010	signalling	positive regulation of growth rate	102, 131, 150, 16, 171, 174, 203, 216, 232, 242, 255, 259, 2, 279, 46, 71, 82, 84, 92, 97
GO:0040017	signalling	positive regulation of locomotion	46
GO:0040018	morphology	positive regulation of multicellular organism growth	114, 174, 19
GO:0040020	morphology	regulation of meiosis	276
GO:0040026	morphology	positive regulation of vulval development	180
GO:0040034	morphology	regulation of development, heterochronic	114
GO:0040035	morphology	hermaphrodite genitalia development	120, 16, 171, 92
GO:0042048	neuron	olfactory behavior	55
GO:0042051	neuron	compound eye photoreceptor development	46
GO:0042063	neuron	gliogenesis	37
GO:0042074	morphology	cell migration involved in gastrulation	60
GO:0042127	morphology	regulation of cell proliferation	276
GO:0042332	signalling	gravitaxis	6
GO:0042673	neuron	regulation of retinal cone cell fate specification	82
GO:0042676	neuron	compound eye cone cell fate commitment	82
GO:0042745	morphology	circadian sleep/wake cycle	6
GO:0042749	morphology	regulation of circadian sleep/wake cycle	6

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0042803	signalling	protein homodimerization activity	155, 32, 37
GO:0042981	signalling	regulation of apoptotic process	134
GO:0043005	neuron	neuron projection	6
GO:0043053	signalling	dauer entry	113
GO:0043066	signalling	negative regulation of apoptotic process	32
GO:0043086	signalling	negative regulation of catalytic activity	153
GO:0043152	signalling	induction of bacterial agglutination	2
GO:0043282	muscle	pharyngeal muscle development	71
GO:0043401	signalling	steroid hormone mediated signaling pathway	114
GO:0043524	neuron	negative regulation of neuron apoptotic process	51
GO:0043620	regulation	regulation of DNA-dependent transcription in response to stress	60
GO:0045087	signalling	innate immune response	233
GO:0045165	morphology	cell fate commitment	37
GO:0045179	signalling	apical cortex	82
GO:0045214	signalling	sarcomere organization	16, 5
GO:0045468	neuron	regulation of R8 cell spacing in compound eye	37
GO:0045475	neuron	locomotor rhythm	6
GO:0045500	neuron	sevenless signaling pathway	46
GO:0045572	signalling	positive regulation of imaginal disc growth	102
GO:0045664	neuron	regulation of neuron differentiation	82
GO:0045676	neuron	regulation of R7 cell differentiation	82
GO:0045746	signalling	negative regulation of Notch signaling pathway	32
GO:0045793	signalling	positive regulation of cell size	120
GO:0045892	regulation	negative regulation of transcription, DNA-dependent	37
GO:0045893	regulation	positive regulation of transcription, DNA-dependent	102
GO:0045900	regulation	negative regulation of translational elongation	285
GO:0045944	signalling	positive regulation of transcription from RNA polymerase II promoter	101, 114, 155
GO:0045980	signalling	negative regulation of nucleotide metabolic process	153
GO:0046008	signalling	regulation of female receptivity, post-mating	2
GO:0046331	signalling	lateral inhibition	18
GO:0046488	signalling	phosphatidylinositol metabolic process	14, 2
GO:0046692	signalling	sperm competition	2
GO:0046716	muscle	muscle cell homeostasis	16, 5
GO:0046843	morphology	dorsal appendage formation	32
GO:0046854	signalling	phosphatidylinositol phosphorylation	14, 2
GO:0046928	neuron	regulation of neurotransmitter secretion	31
GO:0046982	signalling	protein heterodimerization activity	101, 37
GO:0046983	signalling	protein dimerization activity	2
GO:0047291	signalling	lactosylceramide alpha-2, 3-sialyltransferase activity	3
GO:0048102	signalling	autophagic cell death	323, 32
GO:0048190	morphology	wing disc dorsal/ventral pattern formation	323, 37
GO:0048311	regulation	mitochondrion distribution	54
GO:0048368	morphology	lateral mesoderm development	3
GO:0048477	morphology	oogenesis	114, 32
GO:0048488	neuron	synaptic vesicle endocytosis	134, 46
GO:0048500	signalling	signal recognition particle	285
GO:0048512	morphology	circadian behavior	6
GO:0048514	morphology	blood vessel morphogenesis	63
GO:0048644	muscle	muscle organ morphogenesis	5
GO:0048666	neuron	neuron development	37
GO:0048676	neuron	axon extension involved in development	203
GO:0048738	muscle	cardiac muscle tissue development	16
GO:0048741	muscle	skeletal muscle fiber development	71
GO:0048749	neuron	compound eye development	32, 37, 51
GO:0048752	morphology	semicircular canal morphogenesis	174
GO:0048755	neuron	branching morphogenesis of a nerve	3

GO-ID	classification	GO description	internal COP-ID (ake-###)
GO:0048812	neuron	neuron projection morphogenesis	3
GO:0048813	neuron	dendrite morphogenesis	37, 51, 82
GO:0048844	morphology	artery morphogenesis	6
GO:0048846	neuron	axon extension involved in axon guidance	14
GO:0048854	neuron	brain morphogenesis	37, 55
GO:0048885	neuron	neuromast deposition	82
GO:0048886	neuron	neuromast hair cell differentiation	82
GO:0048920	neuron	posterior lateral line neuromast primordium mi- gration	162
GO:0050768	neuron	negative regulation of neurogenesis	37
GO:0050771	signalling	negative regulation of axonogenesis	82
GO:0050790	signalling	regulation of catalytic activity	3, 63
GO:0050830	signalling	defense response to Gram-positive bacterium	153
GO:0050909	signalling	sensory perception of taste	82
GO:0050914	signalling	sensory perception of salty taste	3
GO:0051124	neuron	synaptic growth at neuromuscular junction	31
GO:0051216	morphology	cartilage development	174, 3
GO:0051260	signalling	protein homooligomerization	3
GO:0051403	signalling	stress-activated MAPK cascade	155
GO:0051608	signalling	histamine transport	64
GO:0055002	muscle	striated muscle cell development	71
GO:0055059	neuron	asymmetric neuroblast division	82
GO:0055060	neuron	asymmetric neuroblast division resulting in gan- glion mother cell formation	82
GO:0060028	neuron	convergent extension involved in axis elongation	400, 60
GO:0060029	morphology	convergent extension involved in organogenesis	60
GO:0060037	morphology	pharyngeal system development	174
GO:0060041	neuron	retina development in camera-type eye	64
GO:0060052	neuron	neurofilament cytoskeleton organization	51
GO:0060385	neuron	axonogenesis involved in innervation	82
GO:0060438	morphology	trachea development	174
GO:0060857	neuron	establishment of glial blood-brain barrier	152
GO:0060971	morphology	embryonic heart tube left/right pattern formation	3
GO:0061327	morphology	anterior Malpighian tubule development	174
GO:0070278	signalling	extracellular matrix constituent secretion	174
GO:0070527	signalling	platelet aggregation	3
GO:0070829	signalling	heterochromatin maintenance	155
GO:0070983	neuron	dendrite guidance	82
GO:0071436	signalling	sodium ion export	24, 3
GO:0071470	signalling	cellular response to osmotic stress	155
GO:0071688	muscle	striated muscle myosin thick filament assembly	203, 5
GO:0071805	signalling	potassium ion transmembrane transport	144, 26
GO:0072320	signalling	volume-sensitive chloride channel activity	19
GO:0072583	signalling	clathrin-mediated endocytosis	46
GO:0090305	signalling	nucleic acid phosphodiester bond hydrolysis	131
GO:2000223	signalling	regulation of BMP signaling pathway involved in heart jogging	3

Table S5. Supplementary Table related to Figures 1 and 5. Description of the 85 clusters in set L' .

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	Supplementary Reference	
			Fly					Fish					Worm	
Morphology related														
ake-114	FBgn0000448, FBgn0000568	Hr46, Eip75B	Hormone receptor-like in 46, Ecdysone-induced protein 75B	DHR3, ecdysone-inducible gene product involved in metamorphosis	ENSDARG00000043059	VDR	vitamin D receptor		WBGene00003622	nhr-23	nuclear hormone receptor homolog	required in all larval molts for hypodermal expression and restricted to epidermal cells	[177, 113, 60, 112, 42]	
ake-46	FBgn0000414	Dab	Disabled		ENSDARG00000053091, ENSDARG00000031761	Dab2, BDP1	disabled homolog 2, subunit of RNA polymerase III transcription initiation factor IIIB		WBGene00000894	dab-1	disabled ortholog	required for normal molting and meiotic arrest	[189, 65, 33, 63, 108, 156, 164]	
ake-179	FBgn0264490	Eip93F	Ecdysone-induced protein 93F		ENSDARG00000070907	lcor	ligand dependent nuclear receptor corepressor		WBGene00011315	mbr-1			[13, 184, 56, 150]	
ake-174	FBgn0026562	sparc	BM-40-SPARC		ENSDARG00000019353, ENSDARG00000074989	sparc, sparcl1	secreted cysteine rich glycoprotein, SPARC-like 1		WBGene00003893	ost-1	ortholog of the conserved basement membrane glycoprotein component osteonectin/-SPARC/BM-40 collagen	required for embryonic and larval development	[97, 18, 180, 58, 27, 200, 135]	
ake-14	FBgn0259244				ENSDARG00000037845, ENSDARG00000039462, ENSDARG00000040118, ENSDARG00000054753, ENSDARG00000058960, ENSDARG00000060893, ENSDARG00000068218, ENSDARG00000076163	Col9a3, col10a1, col8a2, otolin 1	collagen		WBGene00000708	col-135			[111, 45, 3, 109]	
ake-101	FBgn0039411	dys	dysfusion		ENSDARG00000055752, ENSDARG00000061920, ENSDARG00000087753	npas4	neuronal PAS domain protein 4 (a, b)		WBGene00000521	cky-1	encodes a member of the basic helix-loop-helix/Per-Arnt-Sim (bHLH-PAS) protein family		[101, 102]	
ake-63	FBgn0035308				ENSDARG00000040614, ENSDARG00000076480, ENSDARG00000040614	Sestd1, mcf2l	SEC14 and spectrin domains, mcf.2 cell line derived transforming sequence-like b		WBGene00010111, WBGene00018887, WBGene00194671				[144, 214]	
ake-32	FBgn0259176	bun	bunched		ENSDARG00000038306, ENSDARG00000075666	Tsc22d 3)	(1, TSC22 domain family, member (1, 3)		WBGene00016272, WBGene00011824				[64, 69, 7, 107]	
Muscle related														
ake-16	FBgn0004028	wupA	wings up A	troponin I (TnI)	ENSDARG00000005841, ENSDARG00000013752, ENSDARG00000029069, ENSDARG00000029995, ENSDARG00000035958, ENSDARG00000042559, ENSDARG00000045592, ENSDARG00000052708, ENSDARG00000073766	tnni 2a.2, troponin I, skeletal, 2a.3, 2a.4, tal, fast, tandem 2b.2, 2b.1, duplicate 1c, 2a.1, 1b, 1d)			WBGene00006584, Tni-WBGene00006585, (1,3,4), WBGene00006586, unc-76 WBGene00006764	troponin I	encodes a member of the troponin family that affects body morphology, locomotion, egg laying, and epithelial morphogenesis	[37, 190, 73, 80, 157, 137, 132, 154, 88, 61, 194, 152]		

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-5	FBgn0004169	up	upheld	troponin (TnT)	T ENSDARG00000002988, ENSDARG000000030270, ENSDARG000000037954, ENSDARG000000045822, ENSDARG000000068457	tnnt (2d, 3a, 2e, 3b)	Troponin T (2d, 2e -cardiac; 3a, 3b -skeletal; typ 1 -skeletal)		WBGene000006588	Tnt-3	troponin T	orthologous to the human gene TROPONIN T (TNNT2; OMIM:191045), which when mutated leads to disease	[37, 190, 73, 80, 157, 137, 132, 154, 88, 61, 194, 152]
ake-71	FBgn0002922	nau	nautilus		ENSDARG00000007277, ENSDARG000000029830, ENSDARG000000030110	Myf (5, 6, d1)	myogenic factor (5, 6, d1)		WBGene000001948	hlh-1	ortholog of the myogenic regulatory factor (MRF) subgroup of basic helix-loop-helix (bHLH) transcription factor	required during embryogenesis for proper muscle development and function, but not for bodywall muscle cell fate specification	[54, 8, 30, 12, 4, 143, 208, 125, 195, 170]
ake-33	FBgn0003016	osp	outspread		ENSDARG000000006385, ENSDARG000000073998, ENSDARG000000074705	Triobp, X	TRIO and F-actin binding protein, myosin phosphatase Rho interacting protein		WBGene000008666				[141]
ake-120	FBgn0035411	Girdin	Girdin		ENSDARG000000076189, ENSDARG000000078440	Ccdc88 (b, Aa)	coiled-coil domain containing (88B, 88Aa)		WBGene00013082				[162, 205, 159]
ake-188	FBgn0039869				ENSDARG000000016754	tbca	tubulin cofactor a		WBGene00021475				[103, 222]
ake-225	FBgn0037737	Pnn	Pinin		ENSDARG000000015851	pnn	pinin	desmosome associated protein	WBGene00011308				[204, 104, 210, 89, 90]
ake-169	FBgn0030699				ENSDARG000000010400	lrrfip2	leucine rich repeat (in FLII) interacting protein 2		WBGene00018998	flap-1			[43]
ake-113	FBgn0036196				ENSDARG000000040277, ENSDARG000000075172	Fbxo (32, 25)	F-box protein (32, 25)		WBGene00008439	mfb-1	F-box protein		[41, 99, 72]
ake-144	FBgn0030745				ENSDARG000000024047, ENSDARG000000041562	Tmem38a, X	transmembrane protein 38A, Uncharacterized protein		WBGene00013255, WBGene00013268				[212]
ake-68	FBgn0035772	Sh3beta	SH3-binding, glutamic acid-rich protein		ENSDARG000000021633, ENSDARG000000036878, ENSDARG000000058302	sh3bgr, sh3bgrl2	SH3 domain binding glutamic acid-rich protein, like		WBGene00013666				[140]
								Neuron related					
ake-267	FBgn0030208	PPP4R2r	Protein phosphatase 4 regulatory subunit 2-related protein		ENSDARG000000026540	ppp4r2a	protein phosphatase 4 regulatory subunit 2a		WBGene00017064	Ppfr-2			[17]
ake-251	FBgn0015323	VACHT			ENSDARG000000006356, ENSDARG000000090189	Slc18a3a, X	solute carrier family 18 (vesicular acetylcholine) member 3a, Uncharacterized protein		WBGene000000481, WBGene00006756	Cha-1, unc-17	Cha-1 encodes a choline acetyltransferase that synthesizes acetylcholine, unc-17 encodes a synaptic vesicle acetylcholine transporter (VACHT), share a common promoter	expressed in neurons, and is required for viability, normal growth, locomotion, and sensitivity to acetylcholinesterase inhibitors	[44, 83, 51]

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
Fly					Fish					Worm			
ake-25	FBgn0051057	tau			ENSDARG000000055052, ENSDARG000000087616, ENSDARG000000089314	Mapt (a, b), tau a	microtubule-associated protein (a, b), microtubule-associated protein tau		WBGene000004212	ptl-1	microtubule-binding protein homologous to tau/MAP2/MAP4 subfamily of microtubule-associated proteins	associated with several neurodegenerative disorders	[31, 55, 98, 16, 62, 114]
ake-82	FBgn0004595	pros	prospero		ENSDARG000000041952, ENSDARG000000055158	Prox 1a)	(2, prospero homeobox (2, 1a)		WBGene00000448	Ceh-26	encodes a protein that contains a prospero-related homeodomain		[46, 161, 6, 219]
ake-276	FBgn0039977				ENSDARG000000056235	smndc1	survival motor neuron domain containing 1		WBGene00004891	smr-1			[191]
ake-31	FBgn0041605	cpx	complexin		ENSDARG000000018997, ENSDARG000000061918	cplx2	Complexin 2, like		WBGene00022271	cpx-1			[142, 70, 133, 81, 34, 95, 218]
ake-64	FBgn0260964	Vmat	Vesicular monoamine transporter		ENSDARG000000015110, ENSDARG000000078157	Slc18a2, X	solute carrier family 18 (vesicular monoamine) member 2, solute carrier family 18 (vesicular monoamine transporter) member 1		WBGene00000295	cat-1	encodes a synaptic vesicular monoamine transporter	required for the presence of dopamine and serotonin in nerve terminals	[50]
ake-62	FBgn0040395	Unc-76			ENSDARG000000022260, ENSDARG000000023174, ENSDARG000000073784		fasciculation and elongation protein zeta (1, 2)		WBGene000006808	unc-76	coiled-coil protein that belongs to the FEZ (fasciculation and elongation protein; zyglin/zeta-1) family of proteins	required for normal axonal outgrowth and hence, normal locomotion and is present in all axons throughout development	[119, 199, 10, 67, 38, 15, 139]
ake-37	FBgn0000591, FBgn0002631, FBgn0002633, FBgn0002735, FBgn0032741	E(spl), HLHm5, HLHm7, HLHm-beta, HLH-mgamma, Side	Enhancer of split, E(spl) re-gion transcript m (5, 7, mbeta, m5/.../similar to Deadpan	of	ENSDARG000000007097, ENSDARG000000016363, ENSDARG000000019335, ENSDARG000000068168, ENSDARG000000069675	her (13, 8a, 2.2, 8.2), hes (6, 2.2)	Hairy-related (13, 8a, 8.2), hairy-related 8a, hairy and enhancer of split 2		WBGene00003008				[207, 9, 66, 115, 220, 57, 181, 39, 85]
ake-73	FBgn0032949, FBgn0052225	Lamp1, X			ENSDARG000000077944, ENSDARG000000092610		lysosomal-associated membrane protein 1		WBGene00015471	Imp-2	lysosomal associated membrane glycoprotein transmembrane protein		[68, 59]
ake-21	FBgn0031213, FBgn0034365	Galectin, X			ENSDARG000000092923, ENSDARG000000093059, ENSDARG000000037613, ENSDARG000000044001, ENSDARG000000077850	Galectin, lectin, lgals3l	Galactoside-binding		WBGene00002266, WBGene00002272, WBGene00008284, WBGene00017080, WBGene00002271, WBGene00002270, WBGene00002273, WBGene00002268	Lec-9,8,7,10,5,3			[87]
ake-155	FBgn0050420	Atf-2	Activating transcription factor-2		ENSDARG000000056156, ENSDARG000000074697	Npdc1, X	neural proliferation, differentiation and control 1		WBGene00000277	cab-1		involved in synaptic regulation	[1]

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-6	FBgn0030437, FBgn0033932, FBgn0052843, FBgn0260753	Hector, Dh44-R1, Dh31-R1, Pdfr	Hector, Diuretic hormone (44, 31) receptor /Pigment-dispersing factor receptor	Diuretic hormone 31 receptor /Pigment-dispersing factor receptor	ENSDARG00000003989, ENSDARG00000006678, ENSDARG00000011473, ENSDARG00000011571, ENSDARG00000018418, ENSDARG00000020957, ENSDARG00000021186, ENSDARG00000028845, ENSDARG00000062377	Crhr1, pth2r, calcrla, calcrlb, pth1rb, pthlra, calcr	corticotropin, parathyroid, calcitonin hormone receptor		WBGene00007664, WBGene00014035		G-protein-coupled receptor (GPCR) that is a member of the secretin family		[44, 197, 117, 25, 100, 145]
ake-203	FBgn0036641	Smn	survival motor neuron		ENSDARG00000018494	smn1	survival motor neuron 1		WBGene00004887	smn-1	encodes a homolog of human cle SMN		[53]
ake-51	FBgn0259108	futsch			ENSDARG00000022045, ENSDARG00000059601, ENSDARG00000060326, ENSDARG00000060434, ENSDARG00000060805	map	microtubule-associated protein (1Ab, 1Aa, 1S, 1b)		WBGene00007966, WBGene00009113, WBGene00009306				[79, 94, 175]
ake-26	FBgn0029761, SK		small conductance calcium-activated potassium channel		ENSDARG00000014939, ENSDARG00000019753, ENSDARG00000023546, ENSDARG00000091306	Kcnn1b, 3)	(1a, potassium intermediate/small conductance calcium-activated channel subfamily N member (2, 3, 1b, 1a)		WBGene00008570	Kcnnl-2			[47]

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-3	FBgn0034286, Dpr (13, 15, 6, 17, 8, 11, 7)			defective proboscis extension response	ENSDARG00000015607, ENSDARG00000017984, ENSDARG00000028912, ENSDARG00000029838, ENSDARG00000034092, ENSDARG00000034466, ENSDARG00000040669, ENSDARG00000041828, ENSDARG00000043445, ENSDARG00000045875, ENSDARG00000053027, ENSDARG00000054655, ENSDARG00000055245, ENSDARG00000057013, ENSDARG00000057886, ENSDARG00000058564, ENSDARG00000070065, ENSDARG00000070223, ENSDARG00000071050, ENSDARG00000076144, ENSDARG00000076981, ENSDARG00000078180, ENSDARG00000078824, ENSDARG00000079487, ENSDARG00000086166, ENSDARG00000086301, ENSDARG00000086919, ENSDARG00000087148, ENSDARG00000088811, ENSDARG00000089316, ENSDARG00000089404, ENSDARG00000089710, ENSDARG00000089993, ENSDARG00000090329, ENSDARG00000090874, ENSDARG00000091074, ENSDARG00000091388, ENSDARG00000091579, ENSDARG00000091661, ENSDARG00000091712, ENSDARG00000092031, ENSDARG00000092322, ENSDARG00000092520, ENSDARG00000093279, ENSDARG00000093880, ENSDARG00000093987, ENSDARG00000094374, ENSDARG00000094391, ENSDARG00000094524, ENSDARG00000095133, ENSDARG00000095134, ENSDARG00000095772	cadm3, unknown	cell adhesion molecule 3, Uncharacterized proteins	WBGene00007851, Clec-4E (245, 126, 122, 121), WBGene00006985	predicted secreted proteins	se-1 member of the immunoglobulin superfamily	[155, 71]		
ake-162	FBgn0039155	kal-1	Kallmann syndrome ortholog	1	ENSDARG00000004932, ENSDARG00000012896, ENSDARG00000087064	Kal1 (b, a)	Kallmann syndrome 1 (b, a) sequence	WBGene00002181	kal-1	cell surface protein that contains a WAP-type inhibitor domain and Type III fibronectin domains	ortholog of human KAL-1, required for epithelial morphogenesis and axon branching	[178, 202]	
ake-84	FBgn0037443				ENSDARG00000046007, ENSDARG00000060954	Tmcc2, X	transmembrane and coiled-coil domain family (2, 1b)	WBGene00015800				[221, 84]	

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-24	FBgn0030638, FBgn0030756				ENSDARG00000009131, ENSDARG00000030588, ENSDARG00000095660	Slc10a (4, solute carrier family 10 (sodium/bile acid cotransporter family) member (4, 3, 1)			WBGene00022135				[120, 167]
ake-112	FBgn0035103, FBgn0042101	Vdup1, X	Vitamin D[[3]] up-regulated protein 1		ENSDARG00000032444, ENSDARG00000067664		Uncharacterized proteins		WBGene00013043	arrd-16			[123, 28]
ake-224	FBgn0032221				ENSDARG00000035175	schip1	schwannomin interacting protein 1		WBGene00018074				[74, 134]
ake-334	FBgn0035676				ENSDARG00000000588	grasp	GRP1 (general receptor for phosphoinositides 1)-associated scaffold protein		WBGene00009272				[110]
Signalling related													
ake-74	FBgn0035028	start1			ENSDARG00000017809, ENSDARG00000074280	Stard3, X	START domain containing 3, StAR-related lipid transfer (START) domain containing 4		WBGene00017826, WBGene0001050				[11, 176]
ake-134	FBgn0261722	fwe	flower		ENSDARG00000090818		calcium channel flower domain containing 1		WBGene00008973				[173, 168, 122, 129]
ake-152	FBgn0039014				ENSDARG00000057322	tmem47	transmembrane protein 47		WBGene00006875	vab-9	claudin homolog Claudins are orthologous tegral membrane proteins with human proteins with brain cell membrane four transmembrane protein 1 brane sequences (BCMP1)		[185, 91, 186]
ake-52	FBgn0015558, FBgn0261444	tty	tweety		ENSDARG00000007678, ENSDARG00000010727, ENSDARG00000016934, ENSDARG00000034473	Ttyh (3b, 2 3a)	(3b, 2, 2 like, 3a)		WBGene00009632	ttyh-1			[23, 138]
ake-18	FBgn0029506, FBgn0033124, FBgn0033127, FBgn0033128, FBgn0033129, FBgn0033130, FBgn0033133, FBgn0033134, FBgn0033135, FBgn0043550	Tsp42E (e, c, f, 42E (e, c, f, g, g, h, i, h, i, k, l, n), k, l, n), Tsp68C	Tetraspanin (e, c, f, 42E (e, c, f, g, g, h, i, h, i, k, l, n), k, l, n), Tetraspanin 68C		ENSDARG00000015015, ENSDARG00000025757, ENSDARG00000068233	Tspan18b, X, X	tetraspanin 18b, X, CD53 molecule		WBGene00006637, WBGene00006643, WBGene00006635, WBGene00006642, WBGene00006641, WBGene00006639	Tsp-(11, 17, 9, 16, 15, 13)			[93, 149, 29, 148]

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
	Fly				Fish				Worm				
ake-19	FBgn0035696, Best 1)	(2, Bestrophin 1)	(2, Bestrophin 2/1)		ENSDARG00000078331, Best 1), 4, Bestrophin (1, 4, 2) ENSDARG00000078455, 2) ENSDARG00000079163				WBGene00015288, orthologous to the human gene VITELLIFORM MACULAR DYSTROPHY PROTEIN (VMD2) WBGene00007404, WBGene00015628, WBGene00007808, WBGene00007988, WBGene00008185, WBGene00008186, WBGene00008821, WBGene00011258, WBGene00020559, WBGene00011868, WBGene00021368, WBGene00013520, WBGene00013921, WBGene00022797, WBGene00014102, WBGene00014103			[35, 36, 193]	
ake-22	FBgn0037913	fabp	fatty acid bindin protein		ENSDARG00000007697, Fabp(7a, 3, fatty acid bind- ENSDARG00000023290, 7b) crabp1 ing protein (7 ENSDARG00000034650, (b, a) - brain, 3 - ENSDARG00000035904, muscle), cellular ENSDARG00000045926 retinoic acid binding protein 1 (a, b)			WBGene00002259, Lbp-(7, intracellular predicted to WBGene00002260, 8, 6, 5, fatty acid bind- function as an WBGene00002258, 9) ing protein intracellular WBGene00002257, (iFABP) protein transporter for WBGene00021486 small hydropho- bic molecules such as lipids and steroid hormones			[2, 151, 147]		
ake-102	FBgn0036318		Wbp2 ortholog		ENSDARG00000056605	Wbp2	WW domain binding protein 2		WBGene00015955, WBGene00008404				[223]
ake-180	FBgn0021818	cnk	connector en- hancer of ksr		ENSDARG00000074236				WBGene00000564	cnk-1	protein that con- tains a SAM do- main, a PDZ do- main, and a PH domain		[40, 20, 198, 174]
ake-285	FBgn0038808	Srp14	Signal recog- nition particle protein 14		ENSDARG00000088272	srp14	signal recogni- tion particle 14		WBGene00017799				[49, 14]
ake-401	FBgn0030711				ENSDARG00000021112	c1d	C1D nuclear receptor co- repressor		WBGene00021785				[215]
ake-55	FBgn0032156, FBgn0034181				ENSDARG00000042892	paip1	poly(A) binding protein interact- ing protein 1		WBGene00018405				[130]
ake-60	FBgn0033166	Eaf	ELL-associated factor		ENSDARG00000010432, Eaf (2, 1) ENSDARG00000070795		ELL associated factor (2, 1)		WBGene00017011	eaf-1			[187, 126, 21, 22, 19, 118, 169, 131, 127] [171]
ake-400	FBgn0035148				ENSDARG00000059177	tax1bp3	Tax1 (human T-cell leukemia virus type I) binding protein 3		WBGene00016678				
ake-20	FBgn0034345				ENSDARG00000013655, Tpd52l (1, tumor protein ENSDARG00000027154, 2b, 2a) ENSDARG00000042548		D52-like (2b, 2a, 1)		WBGene00008745				[24]
ake-92	FBgn0037299				ENSDARG00000028391, vps37 ENSDARG00000031836, vacuolar protein ENSDARG00000039319 sorting 37 ho- molog (B, C)				WBGene00016990	vps-37	endosomal sort- ing ESCRT-I complex that functions in endosomal sorting of mono- ubiquitinated membrane proteins		[160, 76]
ake-233	FBgn0036847				ENSDARG00000070512	tnrc5	trinucleotide re- peat containing 5		WBGene00007531				[203]

...Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-142	FBgn0036090				ENSDARG00000036064	Cnep1r1	CTD nuclear envelope phosphatase 1 regulatory subunit 1		WBGene00011828				[77]
ake-54	FBgn0262872	milt	milton		ENSDARG00000041304, ENSDARG00000078872	trak2	Regulation related trafficking protein kinesin binding (2, 1)		WBGene00020838				[98, 121, 201]
ake-11	FBgn0034067, FBgn0039648, FBgn0261534		l(2)34Fc lethal (2) 34Fc		ENSDARG00000060622, ENSDARG00000069103, ENSDARG00000093957		ferric-chelate reductase 1 like		WBGene00007339, WBGene00007545, WBGene00013292				[166]
ake-118	FBgn0011455		l(3)neo18 lethal (3) neo18		ENSDARG00000070824	ndufb5	NADH dehydrogenase (ubiquinone) 1 beta subcomplex 5		WBGene00016118	ortholog of the NDUFB5/SGDH subunit of the mitochondrial NADH dehydrogenase (ubiquinone) complex (complex I)			[192, 163]
ake-131	FBgn0262116				ENSDARG00000069336, ENSDARG00000069336, ENSDARG00000069461	Rnasek (b, a)	(b, ribonuclease, RNase K (b, a)		WBGene00016721, WBGene00009881				[106]
ake-135	FBgn0032833, FBgn0033020		Cytochrome c oxidase subunit IV		ENSDARG00000022509, ENSDARG00000032970	Cox4i (2, 1)	Cytochrome c oxidase subunit IV isoform (2, 1)		WBGene00012354				[146, 92, 183, 5, 165]
ake-150	FBgn0260407	mRpS23	mitochondrial Ribosomal protein S23		ENSDARG00000033973	Mrps23	mitochondrial ribosomal protein S23		WBGene00014224				[179, 158, 26, 136, 188]
ake-153	FBgn0040660				ENSDARG00000044092, ENSDARG00000067975	Atpif1 (b, a)	(b, ATPase inhibitory factor 1 (b, a)		WBGene00015248	mai-2	orthologous to blocks reverse mitochondrial action (ATP intrinsic ATP-hydrolysis) by F(0)F(1)-Pase inhibitor protein IF(1)) ATPase when its (normally required) proton gradient is lost		[32, 96, 182]
ake-170	FBgn0033373				ENSDARG00000007181	nadk2	NAD kinase 2		WBGene00012463				[86]
ake-171	FBgn0053051				ENSDARG00000012044, ENSDARG00000024687	polr3gla, polr3g	mitochondrial polymerase (RNA) III (DNA directed) polypeptide G, like a		WBGene00021638				[206, 172, 209]
ake-216	FBgn0260460	mRpS34	mitochondrial ribosomal protein S34		ENSDARG00000057910	mrps34	mitochondrial ribosomal protein S34		WBGene00010905				[179, 158, 26, 136, 188]
ake-232	FBgn0037566	mRpL1	mitochondrial ribosomal protein L1		ENSDARG00000054606	mrpl1	mitochondrial ribosomal protein L1		WBGene00017997				[179, 158, 26, 136, 188]
ake-242	FBgn0031357	mRpL48	mitochondrial ribosomal protein L48		ENSDARG00000035167	mrpl48	mitochondrial ribosomal protein L48		WBGene00016989				[179, 158, 26, 136, 188]
ake-255	FBgn0038426	mRpS33	mitochondrial ribosomal protein S33		ENSDARG00000020015	mrps33	mitochondrial ribosomal protein S33		WBGene00009013				[179, 158, 26, 136, 188]
ake-259	FBgn0032053	mRpL51	mitochondrial ribosomal protein L51		ENSDARG00000041340		mitochondrial ribosomal protein L51		WBGene00011740				[179, 158, 26, 136, 188]

... Table S5 continued

internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
	Fly				Fish				Worm				
ake-97	FBgn0034986	mRpS17	mitochondrial ribosomal protein S17		ENSDARG000000054164		mitochondrial ribosomal protein S17		WBGene00015487				[179, 158, 26, 136, 188]
ake-327	FBgn006411				ENSDARG000000056855		glutamyl-tRNA(Gln) amidotransferase subunit C		WBGene00013433				[52, 153]
ake-160	FBgn0038400				ENSDARG000000039374		apolipoprotein O-like		WBGene00019333	moma-1			[78]
ake-217	FBgn0025820	JTBR			ENSDARG000000070150		jumping translocation breakpoint		WBGene00002180	jtr-1	predicted trans-membrane protein that is related to the conserved jumping translocation breakpoint (JTB) family of proteins		[105]
ake-323	FBgn0037700				ENSDARG000000059357	sarnp	SAP domain containing ribonucleoprotein		WBGene00021813				[116, 213]
ake-193	FBgn0032200				ENSDARG000000040822, ENSDARG000000086461	Fundc 2)	(1, FUN14 domain containing (1, 2)		WBGene00011528				[211, 128]
					Others								
ake-184	FBgn0031413				ENSDARG000000086655, ENSDARG000000089374		chromosome 3 open reading frame 83		WBGene00021131				
ake-185	FBgn0032488				ENSDARG000000020611		chromosome 19 open reading frame 47		WBGene00010002				

... Table S5 continued

Internal ID	Flybase ID	Symbol	Name	Description	Ensembl ID	Symbol	Name	Description	Wormbase ID	Symbol	Name	Description	References in Supplementary
			Fly				Fish				Worm		
ake-2	FBgn0016675, Lectin- FBgn0031273, (galC1, FBgn0031910, 46Ca, FBgn0040093, 30A, FBgn0040097, 28C, FBgn0040099, 24Db, FBgn0040102, 24A, FBgn0040104, 21Cb, FBgn0040106, 21Ca, FBgn0040107, 27Da, FBgn0053532, 37Db, FBgn0053533, 22C), FBgn0259230, Sfp24F FBgn0259958, FBgn0262357	Galactose- specific C-type lectin, lectin- (46Ca, 30A, 28C, 24Db, 24A, 21Cb, 21Ca, 27Da, 37Db, 22C), Seminal fluid protein 24F	ENSDARG00000014624, ENSDARG000000021678, ENSDARG000000027399, ENSDARG000000034330, ENSDARG000000036745, ENSDARG000000038551, ENSDARG000000041159, ENSDARG000000041389, ENSDARG000000043736, ENSDARG000000043768, ENSDARG000000043769, ENSDARG000000045867, ENSDARG000000053113, ENSDARG000000058023, ENSDARG000000067495, ENSDARG000000070414, ENSDARG000000070850, ENSDARG000000070851, ENSDARG000000075003, ENSDARG00000007503, ENSDARG000000075634, ENSDARG000000076541, ENSDARG000000077136, ENSDARG000000077692, ENSDARG000000078750, ENSDARG000000079039, ENSDARG000000079107, ENSDARG000000086100, ENSDARG000000087115, ENSDARG000000088252, ENSDARG000000088614, ENSDARG000000088919, ENSDARG000000089758, ENSDARG000000090092, ENSDARG000000091095, ENSDARG000000091460, ENSDARG000000092749, ENSDARG000000092837, ENSDARG000000093391, ENSDARG000000093673, ENSDARG000000093909, ENSDARG000000094184, ENSDARG000000094225, ENSDARG000000094453, ENSDARG000000094750, ENSDARG000000095091, ENSDARG000000095335, ENSDARG000000095481, ENSDARG000000095757, ENSDARG00000013489	ly75, Un- lymphocyte charac- antigen 75, Un- terized characterized proteins proteins	WBGene00015631, Clec-(89, WBGene00009517, 167, 166, WBGene00009518, 172, 209, WBGene00018910, 174, 83, WBGene00044719, 84, 210, WBGene00021224, 187, 186) WBGene00021580, WBGene00021879, WBGene00021895, WBGene00023484, WBGene00022261, WBGene00014137, WBGene00014138	[196]							
ake-279	FBgn0030061				ENSDARG00000009443, ENSDARG00000030357	gltscr2	glioma tumor suppressor can- didate region gene 2	WBGene00012692	[216, 217]				
ake-27	FBgn0000078	Amy-d	Amylase distal					WBGene00008220	[82]				

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