

Knock out of specific maternal vitellogenins in zebrafish (*Danio rerio*) evokes vital changes in egg proteomic profiles that resemble the phenotype of poor quality eggs

Ozlem Yilmaz^{12*}, Amelie Patinote¹, Emmanuelle Com³⁴, Charles Pineau³⁴, Julien Bobe¹

¹ INRAE, LPGP, 35000, Rennes, France.

²Institute of Marine Research, Austevoll Research Station, Storebø, Norway

³Univ Rennes, Inserm, EHESP, Irset-UMR_S 1085, F-35042 Rennes cedex, France

⁴Protim, Univ Rennes, F-35042 Rennes cedex, France

* Correspondence: ozlem.yilmaz@hi.no

Table S1. Proteins differentially regulated in the vtg1-KO experiment. List of the 126 proteins from the vtg1-KO experiment that were considered to be differentially regulated between wild type (WT) and vtg1-KO eggs and whose distribution among various functional categories is illustrated in Fig 1a. These include proteins detected only in wt-type eggs (unique in WT, N=3), proteins detected only in vtg1-KO eggs (down-regulated in KO, N=30), proteins detected only in vtg1-KO eggs (unique in KO, N=5), and proteins detected in vtg1-KO eggs with wt-N-SC 1.5-fold relative to values for WT eggs (up-regulated in KO, N=75). For each protein, the Ensembl Protein ID and associated gene, transcript and protein name, functional category, Regulation (compared to WT) (unique, up-regulated in KO, or down-regulated in KO), and fold-difference in N-SC between groups (if available) is shown. Color shading corresponds to that used to designate functional categories in Fig 1.

Ensembl Protein ID	Associated Gene Name	Associated Transcript Name	Protein full name	Functional Category	Regulation (compared to WT)	Fold Difference
1 ENSDARP00000101309	vtg1	vtg1-201	Vitellogenin 4	Vitellogenins	unique in WT	-
2 ENSDARP00000115014	vtg1	vtg1-204	Vitellogenin 4	Vitellogenins	unique in WT	-
3 ENSDARP00000072738	vtg1	vtg1-001	Vitellogenin 1	Vitellogenins	down-regulated in KO	1427.37
4 ENSDARP00000050237	vtg1	vtg1-001	Vitellogenin 1	Vitellogenins	down-regulated in KO	1150.36
5 ENSDARP00000072687	vtg1	vtg1-001	Vitellogenin 5	Vitellogenins	down-regulated in KO	26.1
6 ENSDARP00000109480	vtg5	vtg5-202	Vitellogenin 5	Vitellogenins	down-regulated in KO	18.55
7 ENSDARP00000013402	cat	cat-201	Catalase	Redox/Detox related	down-regulated in KO	4.53
8 ENSDARP00000107673	cat	cat-202	Catalase	Redox/Detox related	down-regulated in KO	4.53
9 ENSDARP00000040396	prdx2	prdx2-201	Peroxiredoxin 2	Redox/Detox related	down-regulated in KO	3.57
10 ENSDARP00000124779	cat	cat-001	Catalase	Redox/Detox related	down-regulated in KO	3.13
11 ENSDARP00000126962	ckbb	ckbb-203	Creatine kinase, brain b	Energy metabolism	down-regulated in KO	2.83
12 ENSDARP00000115226	ckbb	ckbb-204	Creatine kinase, brain b	Energy metabolism	down-regulated in KO	2.83
13 ENSDARP00000115657	ckbb	ckbb-205	Creatine kinase, brain b	Energy metabolism	down-regulated in KO	2.64
14 ENSDARP00000113177	crp	crp-201	C-reactive protein	Immune system related	down-regulated in KO	2.48
15 ENSDARP00000073460	crp2	crp2-203	C-reactive protein 2	Immune system related	down-regulated in KO	2.48
16 ENSDARP00000118605	slc45a4	slc45a4-203	Solute carrier family 45, member 4	Energy metabolism	down-regulated in KO	2.28
17 ENSDARP00000080196	slc45a4	slc45a4-201	Solute carrier family 45, member 4	Energy metabolism	down-regulated in KO	2.27
18 ENSDARP00000097762	sidkey-46g23.2	sidkey-46g23.2-2-202	Alpha-2-macroglobulin-like 1	Protein degradation and synthesis inhibition	down-regulated in KO	2.26
19 ENSDARP00000024900	ckbb	ckbb-201	Creatine kinase, brain b	Energy metabolism	down-regulated in KO	1.90
20 ENSDARP00000016065	hsp90a1.2	hsp90a1.2-2-201	Heat shock protein 90, alpha (cytosolic), class A member 1, tandem duplicate 2	Protein degradation and synthesis inhibition	down-regulated in KO	1.82
21 ENSDARP00000116170	zgic113984	zgic113984-202	SUEL type lectin	Lectins	down-regulated in KO	1.73
22 ENSDARP00000121130	zgic113984	zgic113984-203	SUEL type lectin	Lectins	down-regulated in KO	1.73
23 ENSDARP00000127075	zgic113984	zgic113984-204	SUEL type lectin	Lectins	down-regulated in KO	1.72
24 ENSDARP00000005260	MFAP4 (8 of 14)	MFAP4 (8 of 14)-201	Microfibrillar-associated protein 4	Cell cycle, division, growth and fate	down-regulated in KO	1.69
25 ENSDARP00000126800	ckbb	ckbb-207	Creatine kinase, brain b	Energy metabolism	down-regulated in KO	1.65
26 ENSDARP00000015917	ckba	ckba-201	Creatine kinase, brain a	Energy metabolism	down-regulated in KO	1.61
27 ENSDARP00000012517	ckba	ckba-202	Creatine kinase, brain a	Energy metabolism	down-regulated in KO	1.61
28 ENSDARP00000124582	cnp	cnp-011	2,3-cyclic nucleotide 3, phosphodiesterase	Cell cycle, division, growth and fate	down-regulated in KO	1.58
29 ENSDARP00000124216	cnp	cnp-007	2,3-cyclic nucleotide 3, phosphodiesterase	Cell cycle, division, growth and fate	down-regulated in KO	1.58
30 ENSDARP00000005630	crp2	crp2-201	C-reactive protein 2	Immune response related	down-regulated in KO	1.55
31 ENSDARP00000114321	sidkey-90123.2	sidkey-90123.2-2-203	SUEL type lectin	Lectins	down-regulated in KO	1.52
32 ENSDARP00000116297	sidkey-90123.2	sidkey-90123.2-2-203	SUEL type lectin	Lectins	down-regulated in KO	1.52
33 ENSDARP00000006379	gadh	gadh-201	Glyceraldehyde-3-phosphate dehydrogenase	Energy metabolism	up-regulated in KO	0.65
34 ENSDARP00000002318	gpi3	gpi3-201	Glycosylphosphatidylinositol 3	Vitellogenins	up-regulated in KO	0.62
35 ENSDARP000000013329	ldhba	ldhba-201	Lactate dehydrogenase Ba	Energy metabolism	up-regulated in KO	0.62
36 ENSDARP00000098462	zgic165518	zgic165518-201	Alpha-2-macroglobulin-like 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.62
37 ENSDARP000000011595	gylg1a	gylg1a-201	Glycogenin 1a	Energy metabolism	up-regulated in KO	0.62
38 ENSDARP000000012281	zgic165518	zgic165518-202	Alpha-2-macroglobulin-like 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.62
39 ENSDARP00000094194	vtg3	vtg3-202	Vitellogenin 3, phosphatidyl	Vitellogenins	up-regulated in KO	0.60
40 ENSDARP00000015293	hspa8	hspa8-201	Heat shock protein 8	Protein degradation and synthesis inhibition	up-regulated in KO	0.60
41 ENSDARP00000005233	cp	cp-201	Ceruloplasmin	Redox/Detox related	up-regulated in KO	0.59
42 ENSDARP000000010413	hsp70.3	hsp70.3-201	Heat shock cognate 70-kd protein, tandem duplicate 3	Protein degradation and synthesis inhibition	up-regulated in KO	0.58
43 ENSDARP000000030050	hsp70	hsp70-201	Heat shock cognate 70-kd protein, like	Protein degradation and synthesis inhibition	up-regulated in KO	0.58
44 ENSDARP00000045766	mcm5	mcm5-201	MCM5 minichromosome maintenance deficient 5	Cell cycle, division, growth and fate	up-regulated in KO	0.58
45 ENSDARP000000030050	hsp70.3	hsp70.3-202	Heat shock cognate 70-kd protein, tandem duplicate 2	Protein degradation and synthesis inhibition	up-regulated in KO	0.58
46 ENSDARP000000109159	FP016243.1	FP016243.1-2-201	MCM5 minichromosome maintenance deficient 5	Cell cycle, division, growth and fate	up-regulated in KO	0.58
47 ENSDARP000000128405	vtg6	vtg6-001	Vitellogenin 6, phosphatidyl	Vitellogenins	up-regulated in KO	0.56
48 ENSDARP000000049792	gstm1	gstm1-1-201	Glutathione S-transferase M1	Redox/Detox related	up-regulated in KO	0.55
49 ENSDARP000000069198	notb	notb-201	Noctuid	Protein degradation and synthesis inhibition	up-regulated in KO	0.53
50 ENSDARP000000127005	HSPA8 (1 of many)	HSPA8 (1 of many)-203	Heat shock 70kDa protein 8	Protein degradation and synthesis inhibition	up-regulated in KO	0.49
51 ENSDARP00000128683	ACTG2 (1 of many)	ACTG2 (1 of many)-201	Actin, alpha, cardiac muscle 1	Cell cycle, division, growth and fate	up-regulated in KO	0.48
52 ENSDARP00000007895	nasp	nasp-201	Nuclear autoantigenic sperm protein (histone-binding)	Protein synthesis	up-regulated in KO	0.47
53 ENSDARP000000074169	nme2b.2	nme2b.2-2-201	NME/NM23 nucleoside diphosphate kinase 2b, tandem duplicate 2	Cell cycle, division, growth and fate	up-regulated in KO	0.46
54 ENSDARP000000066429	acta2	acta2-201	Actin, alpha 2, smooth muscle, aorta	Cell cycle, division, growth and fate	up-regulated in KO	0.45
55 ENSDARP000000100195	ACTG2 (1 of many)	ACTG2 (1 of many)-202	Actin, alpha, cardiac muscle 1	Cell cycle, division, growth and fate	up-regulated in KO	0.45
56 ENSDARP000000100195	acta2	acta2-202	Actin, alpha 2, smooth muscle, aorta	Cell cycle, division, growth and fate	up-regulated in KO	0.45
57 ENSDARP000000052837	acta1a	acta1a-201	Actin, alpha 1a, skeletal muscle	Cell cycle, division, growth and fate	up-regulated in KO	0.43
58 ENSDARP000000055135	actc1b	actc1b-201	Actin, alpha, cardiac muscle 1b	Cell cycle, division, growth and fate	up-regulated in KO	0.43
59 ENSDARP000000060744	acta1b	acta1b-201	Actin, alpha 1b, cardiac muscle	Cell cycle, division, growth and fate	up-regulated in KO	0.43
60 ENSDARP000000062369	actc1a	actc1a-201	Actin, alpha 1a, skeletal muscle	Cell cycle, division, growth and fate	up-regulated in KO	0.43
61 ENSDARP000000075110	ACTC1 (1 of many)	ACTC1 (1 of many)-201	Novel actin protein	Cell cycle, division, growth and fate	up-regulated in KO	0.43
62 ENSDARP000000100434	ACTC1 (1 of many)	ACTC1 (1 of many)-202	Novel actin protein	Cell cycle, division, growth and fate	up-regulated in KO	0.43
63 ENSDARP000000069621	hpc	hpc-201	Hydroxyphenylpyruvate carboxylase	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
64 ENSDARP000000063039	atp5b	atp5b-201	ATP synthase, H ⁺ -transporting, mitochondrial F1 complex, beta polypeptide	Energy metabolism	up-regulated in KO	0.42
65 ENSDARP000000009319	nme2b.2	nme2b.2-2-204	NME/NM23 nucleoside diphosphate kinase 2b, tandem duplicate 2	Cell cycle, division, growth and fate	up-regulated in KO	0.41
66 ENSDARP000000009319	gadh	gadh-203	Glyceraldehyde-3-phosphate dehydrogenase	Energy metabolism	up-regulated in KO	0.41
67 ENSDARP000000118100	gadh	gadh-204	Glyceraldehyde-3-phosphate dehydrogenase	Energy metabolism	up-regulated in KO	0.41
68 ENSDARP000000057284	nasp	nasp-202	Nuclear autoantigenic sperm protein (histone-binding)	Protein synthesis	up-regulated in KO	0.40
69 ENSDARP000000116010	vtg7	vtg7-002	Vitellogenin 7	Vitellogenins	up-regulated in KO	0.40
70 ENSDARP000000009679	ubc	ubc-001	Ubiquitin C	Protein degradation and synthesis inhibition	up-regulated in KO	0.37
71 ENSDARP000000030819	sich211-202a12.4-201	sich211-202a12.4-201	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.37
72 ENSDARP000000106956	sich211-202a12.4-202	sich211-202a12.4-202	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.37
73 ENSDARP000000060744	ubas2	ubas2-201	Ubiquitin A52 residue ribosomal protein fusion product 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.37
74 ENSDARP000000088354	ubj	ubj-201	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.37
75 ENSDARP000000107110	rps27a	rps27a-201	Ribosomal protein S27a	Protein synthesis	up-regulated in KO	0.37
76 ENSDARP000000123775	rps27a	rps27a-202	Ribosomal protein S27a	Protein synthesis	up-regulated in KO	0.37
77 ENSDARP000000072678	vtg7	vtg7-201	Vitellogenin 7	Vitellogenins	up-regulated in KO	0.34
78 ENSDARP000000114558	vtg7	vtg7-001	Vitellogenin 7	Vitellogenins	up-regulated in KO	0.34
79 ENSDARP0000000098065	nme2b.2	nme2b.2-2-203	NME/NM23 nucleoside diphosphate kinase 2b, tandem duplicate 2	Cell cycle, division, growth and fate	up-regulated in KO	0.33
80 ENSDARP000000110582	nme2b.2	nme2b.2-2-202	NME/NM23 nucleoside diphosphate kinase 2b, tandem duplicate 2	Cell cycle, division, growth and fate	up-regulated in KO	0.33
81 ENSDARP0000000098065	qdprb2	qdprb2-203	Quinoid dihydropteridine reductase b2	Redox/Detox related	up-regulated in KO	0.33
82 ENSDARP000000038398	p4hb	p4hb-001	Protein disulfide isomerase	Protein degradation and synthesis inhibition	up-regulated in KO	0.32
83 ENSDARP000000103251	qdprb2	qdprb2-201	Quinoid dihydropteridine reductase b2	Redox/Detox related	up-regulated in KO	0.31
84 ENSDARP000000063661	mdr2	mdr2-201	Malate dehydrogenase 2, NAD (mitochondrial)	Energy metabolism	up-regulated in KO	0.28
85 ENSDARP000000002751	ee1a1a	ee1a1a-201	Eukaryotic translation elongation factor 1 alpha 1a	Protein synthesis	up-regulated in KO	0.27
86 ENSDARP000000117259	MFAP4 (12 of 14)	MFAP4 (12 of 14)-201	Microfibrillar-associated protein 4	Cell cycle, division, growth and fate	up-regulated in KO	0.24
87 ENSDARP000000124591	pdia3	pdia3-002	Protein disulfide isomerase family A, member 3	Protein degradation and synthesis inhibition	up-regulated in KO	0.22
88 ENSDARP000000125214	sidkey-98a7.8	sidkey-98a7.8-201	SUEL type lectin	Lectins	up-regulated in KO	0.21
89 ENSDARP000000110519	AL929192.1	AL929192.1-201	uncharacterized	Others	up-regulated in KO	0.21
90 ENSDARP000000007345	sidkey-46g23.5	sidkey-46g23.5-2-202	Alpha-2-macroglobulin-like 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.21
91 ENSDARP000000008576	sidkey-46g23.5	sidkey-46g23.5-2-201	Alpha-2-macroglobulin-like 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.20
92 ENSDARP000000107611	qdprb2	qdprb2-202	Quinoid dihydropteridine reductase b2	Redox/Detox related	up-regulated in KO	0.18
93 ENSDARP000000112476	qdprb2	qdprb2-201	Quinoid dihydropteridine reductase b2	Redox/Detox related	up-regulated in KO	0.18
94 ENSDARP000000024082	atc	atc-201	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	Cell cycle, division, growth and fate	up-regulated in KO	0.15
95 ENSDARP000000125193	bx49337.1	bx49337.1-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
96 ENSDARP000000125238	sidkey-98a7.3	sidkey-98a7.3-202	SUEL type lectin	Lectins	up-regulated in KO	0.15
97 ENSDARP000000125244	sidkey-98a7.3	sidkey-98a7.3-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
98 ENSDARP000000125496	sich211.250b5.9	sich211.250b5.9-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
99 ENSDARP000000120702	sidkey-98a7.4	sidkey-98a7.4-202	SUEL type lectin	Lectins	up-regulated in KO	0.15
100 ENSDARP000000106988	sidkey-98a7.4	sidkey-98a7.4-201	Rhamnose binding lectin-like precursor	Lectins	up-regulated in KO	0.15
101 ENSDARP000000107578	sidkey-98a7.4	sidkey-98a7.4-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
102 ENSDARP000000109226	AL929192.2	AL929192.2-201	uncharacterized	Others	up-regulated in KO	0.15
103 ENSDARP000000111454	sidkey-98a7.5	sidkey-98a7.5-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
104 ENSDARP000000111784	sidkey-98a7.3	sidkey-98a7.3-201	SUEL type lectin	Lectins	up-regulated in KO	0.15
105 ENSDARP000000069823	ee1a1b	ee1a1b-201	Eukaryotic translation elongation factor 1 alpha 1b	Protein synthesis	up-regulated in KO	0.13
106 ENSDARP000000104468	ee1a1a	ee1a1a-202	Eukaryotic translation elongation factor 1 alpha 1a	Protein synthesis	up-regulated in KO	0.13
107 ENSDARP000000118774	ee1a1b	ee1a1b-202	Eukaryotic translation elongation factor 1 alpha 1b	Protein synthesis	up-regulated in KO	0.13
108 ENSDARP000000043687	sidkey-24117.2	sidkey-24117.2-201	C-type lectin	Immune response related	unique in KO	-
109 ENSDARP000000107173	sidkey-24117.5	sidkey-24117.5-201	C-type lectin	Lectins	unique in KO	-
110 ENSDARP000000109765	sidkey-24117.4	sidkey-24117.4-201	C-type lectin	Lectins	unique in KO	-
111 ENSDARP000000127204	sidkey-24117.2	sidkey-24117.2-202	C-type lectin	Lectins	unique in KO	-
112 ENSDARP000000127261	sidkey-24117.4	sidkey-24117.4-202	C-type lectin	Lectins	unique in KO	-
113 ENSDARP000000127328	sidkey-24117.2	sidkey-24117.2-203	C-type lectin	Lectins	unique in KO	-
114 ENSDARP000000127453	sidkey-24117.5	sidkey-24117.5-202	C-type lectin	Lectins	unique in KO	-
115 ENSDARP000000001921	ee1a2	ee1a2-201	Eukaryotic translation elongation factor 1 alpha 2	Protein synthesis	unique in KO	-
116 ENSDARP000000003318	QPR (1 of many)	QPR (1 of many)-201	Quinoid dihydropteridine reductase	Redox/Detox related	unique in KO	-
117 ENSDARP000000003318	serpin1	serpin1-201	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), antitrypsin	Protein degradation and synthesis inhibition	unique in KO	-
118 ENSDARP000000104927	crp2	crp2-204	C-reactive protein 2	Immune response related	unique in KO	-
119 ENSDARP000000107615	serpin1	serpin1-001	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), antitrypsin	Protein degradation and synthesis inhibition	unique in KO	-
120 ENSDARP000000115568	sidkey-46h3.8	sidkey-46h3.8-201	SUEL type lectin	Lectins	unique in KO	-
121 ENSDARP000000116589	crp3	crp3-201	C-reactive protein 3	Immune response related	unique in KO	-
122 ENSDARP000000122542	ddx41	ddx41-201	DEAD (Asp-Glu-Ala-Asp) box polypeptide 41	Immune response related	unique in KO	-
123 ENSDARP000000122730	ddx41	ddx41-202	DEAD (Asp-Glu-Ala-Asp) box polypeptide 41	Immune response related	unique in KO	-
124 ENSDARP00000012406	sidkey-46h3.8	sidkey-46h3.8-201	SUEL type lectin	Lectins	unique in KO	-
125 ENSDARP000000127700	serpin1	serpin1-201	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), antitrypsin	Protein degradation and synthesis inhibition	unique in KO	-
126 ENSDARP000000128898	serpin1	serpin1-202	Serine (or cysteine) proteinase inhibitor, clade A (alpha-1 antitrypsin), antitrypsin	Protein degradation and synthesis inhibition	unique in KO	-

Table S2. Proteins differentially regulated in the vtg3-KO experiment. List of the 74 proteins from the vtg3-KO experiment that were considered to be differentially regulated between wild type (Wt) and vtg3-KO eggs and whose distribution among various functional categories is illustrated in Fig 1b. These include proteins detected only in wild type eggs (unique in Wt, N=9), proteins detected in Wt eggs with N-SC >1.5-fold relative to values for vtg3-KO eggs (down-regulated in KO, N=12), proteins detected only in vtg3-KO eggs (unique in KO, N=1), and proteins detected in vtg3-KO eggs with N-SC >1.5-fold relative to values for Wt eggs (up-regulated in KO, N=52). For each protein, the Ensembl Protein ID and associated gene, transcript and protein name, functional category, Regulation (compared to Wt) (unique, up-regulated in KO, or down-regulated in KO), and fold-difference in N-SC between groups (if available) is shown. Color shading corresponds to that used to designate functional categories in Fig 1.

Ensembl Protein ID	Associated Gene Name	Associated Transcript Name	Protein Full Name	Functional Category	Regulation (compared to Wt)	Fold Difference
1 ENSDARPO00000123153	vtg3	vtg3-201	Vitellogenin 3	Vitellogenins	unique in Wt	-
2 ENSDARPO00000080196	slc45a4	slc45a4-001	Solute carrier family 45, member 4	Energy metabolism	unique in Wt	-
3 ENSDARPO00000089804	zgc136254	zgc136254-001	Phosphatidylinositol-3-phosphate binding activity	Lipid metabolism	unique in Wt	-
4 ENSDARPO00000089806	slch211-251f6.7	slch211-251f6.7-201	Phosphatidylinositol-3-phosphate binding activity	Lipid metabolism	unique in Wt	-
5 ENSDARPO00000041601	vtg3	vtg3-202	Vitellogenin 3	Vitellogenins	unique in Wt	-
6 ENSDARPO00000113985	slch211-251f6.7	slch211-251f6.7-001	Phosphatidylinositol-3-phosphate binding activity	Lipid metabolism	unique in Wt	-
7 ENSDARPO00000128406	vtg3	vtg3-001	Vitellogenin 3, phosvitinless	Vitellogenins	unique in Wt	-
8 ENSDARPO00000128605	slc45a4	slc45a4-201	Solute carrier family 45, member 4	Energy metabolism	unique in Wt	-
9 ENSDARPO00000129497	zgc136254	zgc136254-201	Phosphatidylinositol-3-phosphate binding activity	Lipid metabolism	unique in Wt	-
10 ENSDARPO00000131402	cat	cat-201	Catalase	Redox/Detox related	down-regulated in KO	7.26
11 ENSDARPO00000107673	cat	cat-202	Catalase	Redox/Detox related	down-regulated in KO	7.26
12 ENSDARPO00000124779	cat	cat-001	Catalase	Redox/Detox related	down-regulated in KO	4.97
13 ENSDARPO00000115703	eno3	eno3-005	Enolase 3	Energy metabolism	down-regulated in KO	4.27
14 ENSDARPO00000029296	ee1a11	ee1a11-202	Eukaryotic translation elongation factor 1 alpha 1, like 1	Protein synthesis	down-regulated in KO	2.69
15 ENSDARPO00000111742	ee1a11	ee1a11-203	Eukaryotic translation elongation factor 1 alpha 1, like 1	Protein synthesis	down-regulated in KO	2.69
16 ENSDARPO00000006339	ee1a11	ee1a11-201	Eukaryotic translation elongation factor 1 alpha 1, like 1	Protein synthesis	down-regulated in KO	2.44
17 ENSDARPO00000120742	eno3	eno3-001	Enolase 3	Energy metabolism	down-regulated in KO	2.39
18 ENSDARPO0000017456	hspa5	hspa5-201	Heat shock protein 5	Protein degradation and synthesis inhibition	down-regulated in KO	2.08
19 ENSDARPO00000056380	crp2	crp2-001	C-reactive protein 2	Immune response related	down-regulated in KO	1.80
20 ENSDARPO00000124216	crnp	crnp-007	2'3'-cyclic nucleotide 3, phosphodiesterase	Cell cycle, division, growth and fate	down-regulated in KO	1.72
21 ENSDARPO00000124582	crnp	crnp-011	2'3'-cyclic nucleotide 3, phosphodiesterase	Cell cycle, division, growth and fate	down-regulated in KO	1.72
22 ENSDARPO00000072687	vtg3	vtg3-001	Vitellogenin 3	Vitellogenins	up-regulated in KO	0.67
23 ENSDARPO00000143242	HSP48 (1 of many)	vtg3-001 (1 of many)-001	Heat shock 70kDa protein 8	Protein degradation and synthesis inhibition	up-regulated in KO	0.65
24 ENSDARPO00000114558	vtg7	vtg7-001	Vitellogenin 7	Vitellogenins	up-regulated in KO	0.65
25 ENSDARPO00000072678	vtg7	vtg7-201	Vitellogenin 7	Vitellogenins	up-regulated in KO	0.65
26 ENSDARPO00000128683	ACT1C1 (1 of many)	ACT1C1 (1 of many)-001	Actin, alpha, cardiac muscle 1	Cell cycle, division, growth and fate	up-regulated in KO	0.64
27 ENSDARPO00000107175	slch73-160p18.3	slch73-160p18.3-001	Uncharacterized	Others	up-regulated in KO	0.64
28 ENSDARPO00000124371	acta2	acta2-001	Actin, alpha 2, smooth muscle, aorta	Cell cycle, division, growth and fate	up-regulated in KO	0.64
29 ENSDARPO00000100195	ACTC1 (1 of many)	ACTC1 (1 of many)-002	Actin, alpha, cardiac muscle 1	Cell cycle, division, growth and fate	up-regulated in KO	0.62
30 ENSDARPO00000106480	vtg3	vtg3-001	Vitellogenin 3	Vitellogenins	up-regulated in KO	0.61
31 ENSDARPO00000052837	act1a	act1a-001	Actin, alpha 1a, skeletal muscle	Cell cycle, division, growth and fate	up-regulated in KO	0.60
32 ENSDARPO00000055135	act1b	act1b-201	Actin, alpha, cardiac muscle 1b	Cell cycle, division, growth and fate	up-regulated in KO	0.60
33 ENSDARPO00000058628	act1b	act1b-001	Actin, alpha 1b, skeletal muscle	Cell cycle, division, growth and fate	up-regulated in KO	0.60
34 ENSDARPO00000062369	act1a	act1a-001	Actin, alpha, cardiac muscle 1a	Cell cycle, division, growth and fate	up-regulated in KO	0.60
35 ENSDARPO00000066429	acta2	acta2-201	Actin, alpha 2, smooth muscle, aorta	Cell cycle, division, growth and fate	up-regulated in KO	0.60
36 ENSDARPO00000075110	zgc-86709	zgc-86709-001	Novel actin protein	Cell cycle, division, growth and fate	up-regulated in KO	0.60
37 ENSDARPO00000100434	slch73-187m15.4	slch73-187m15.4-001	Actin, alpha, cardiac muscle 1a	Cell cycle, division, growth and fate	up-regulated in KO	0.60
38 ENSDARPO00000043994	slch211-199o1.2	slch211-199o1.2-201	protein folding chaperone	Protein degradation and synthesis inhibition	up-regulated in KO	0.60
39 ENSDARPO00000073132	hsp70.2	hsp70.2-201	Heat shock cognate 70-kd protein, tandem duplicate 2	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
40 ENSDARPO00000102412	hsp70.1	hsp70.1-201	Heat shock cognate 70-kd protein, like	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
41 ENSDARPO00000010413	hsp70.3	hsp70.3-001	Heat shock cognate 70-kd protein, tandem duplicate 3	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
42 ENSDARPO00000030050	hsp70l	hsp70l-001	Heat shock cognate 70-kd protein, like	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
43 ENSDARPO00000045766	mcm/hsp70.1	mcm5-201	MCM5 minichromosome maintenance deficient 5 (S. cerevisiae)	Cell cycle, division, growth and fate	up-regulated in KO	0.59
44 ENSDARPO00000103854	hsp70.2	hsp70.2-001	Heat shock cognate 70-kd protein, tandem duplicate 2	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
45 ENSDARPO00000109199	mcm/hsp70.1	mcm5-001	MCM5 minichromosome maintenance deficient 5 (S. cerevisiae)	Cell cycle, division, growth and fate	up-regulated in KO	0.59
46 ENSDARPO00000114162	slch211-199o1.2	slch211-199o1.2-001	protein folding chaperone	Protein degradation and synthesis inhibition	up-regulated in KO	0.59
47 ENSDARPO00000105057	sidkeyp-46h3.2	sidkeyp-46h3.2-001	SUEL type Lectin domain	Lectins	up-regulated in KO	0.56
48 ENSDARPO00000113693	sidkeyp-46h3.3	sidkeyp-46h3.3-001	SUEL type Lectin domain	Lectins	up-regulated in KO	0.56
49 ENSDARPO00000122552	ckba	ckba-004	Creatine kinase, brain a	Energy metabolism	up-regulated in KO	0.56
50 ENSDARPO00000059365	ckmb	ckmb-001	Creatine kinase, muscle b	Energy metabolism	up-regulated in KO	0.56
51 ENSDARPO00000117584	ckba	ckba-003	Creatine kinase, brain a	Energy metabolism	up-regulated in KO	0.56
52 ENSDARPO00000037871	ckma	ckma-001	Creatine kinase, muscle a	Energy metabolism	up-regulated in KO	0.56
53 ENSDARPO00000117697	hsp	hsp-001	Nuclear autoantigenic sperm protein (histone-binding)	Protein synthesis	up-regulated in KO	0.56
54 ENSDARPO00000119867	hspa8	hspa8-002	Heat shock protein 8	Protein degradation and synthesis inhibition	up-regulated in KO	0.53
55 ENSDARPO00000005298	chia.4	chia.4-001	Chitinase, acidic.4	Immune response related	up-regulated in KO	0.47
56 ENSDARPO00000013329	ldhba	ldhba-001	Lactate dehydrogenase Ba	Energy metabolism	up-regulated in KO	0.46
57 ENSDARPO00000057284	hsp	hsp-004	Nuclear autoantigenic sperm protein (histone-binding)	Protein synthesis	up-regulated in KO	0.44
58 ENSDARPO00000002844	ahcy	ahcy-001	S-adenosylhomocysteine hydrolase	Protein degradation and synthesis inhibition	up-regulated in KO	0.44
59 ENSDARPO00000030819	slch211-202a12.4	slch211-202a12.4-001	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
60 ENSDARPO00000106956	slch211-202a12.4	slch211-202a12.4-201	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
61 ENSDARPO00000089879	ubc	ubc-001	Ubiquitin C	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
62 ENSDARPO00000060744	uba52	uba52-001	Ubiquitin A-52 residue ribosomal protein fusion product 1	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
63 ENSDARPO00000088354	ubb	ubb-001	Ubiquitin B	Protein degradation and synthesis inhibition	up-regulated in KO	0.42
64 ENSDARPO00000107110	rps27a	rps27a-001	Ribosomal protein S27a	Protein synthesis	up-regulated in KO	0.42
65 ENSDARPO00000128775	rps27a	rps27a-002	Ribosomal protein S27a	Protein synthesis	up-regulated in KO	0.42
66 ENSDARPO00000107746	chia.4	chia.4-202	Chitinase, acidic.4	Immune response related	up-regulated in KO	0.40
67 ENSDARPO00000093898	p4hb	p4hb-001	Protein disulfide-isomerase precursor	Protein degradation and synthesis inhibition	up-regulated in KO	0.36
68 ENSDARPO00000059885	ldha	ldha-201	Lactate dehydrogenase A4	Energy metabolism	up-regulated in KO	0.34
69 ENSDARPO00000127005	HSP48 (1 of many)	HSP48 (1 of many)-003	Heat shock 70kDa protein 8	Protein degradation and synthesis inhibition	up-regulated in KO	0.32
70 ENSDARPO00000124591	pdia3	pdia3-002	Protein disulfide isomerase family A, member 3	Protein degradation and synthesis inhibition	up-regulated in KO	0.31
71 ENSDARPO00000063661	mdh2	mdh2-201	Malate dehydrogenase 2, NAD (mitochondrial)	Energy metabolism	up-regulated in KO	0.29
72 ENSDARPO00000107127	sidkeyp-46h3.6	sidkeyp-46h3.6-001	SUEL-type Lectin	Lectins	up-regulated in KO	0.29
73 ENSDARPO0000018458	pdia4	pdia4-001	Protein disulfide isomerase associated 4	Protein degradation and synthesis inhibition	up-regulated in KO	0.23
74 ENSDARPO00000122652	zgc66313	zgc66313-005	Alpha-amylase	Energy metabolism	unique in KO	-

Table S3. Complete PANTHER overrepresentation analysis for differentially regulated proteins in the *vtgI*-KO experiment

<i>vtgI</i>-KO Experiment: proteins down-regulated in <i>vtgI</i>-KO eggs (Wt; N=32, ≥ 4 samples >1.5 fold)						
Analysis Type: PANTHER Overrepresentation Test (Released 20190711)						
Annotation Version and Release Date: PANTHER version 14.1 Released 2019-03-12						
Reference: Danio rerio						
Test Type: Fisher's Exact						
Correction: Bonferroni correction for multiple testing ($p < 0.05$)						
<i>PANTHER GO-Slim Biological Process</i>	#REF	#Protein	Expected	Fold	+/-	P value
Response to estradiol	23	3	0.01	> 100	+	1.62E-04
Response to organic cyclic compound	34	3	0.01	> 100	+	4.83E-04
Cellular response to chemical stimulus	245	4	0.1	41.29	+	2.58E-03
Unclassified	12906	5	5.1	0.98	-	0.00E+00
<i>PANTHER GO-Slim Molecular Function</i>	#REF	#Protein	expected	Fold	+/-	P value
Lipid transporter activity	120	3	0.05	63.22	+	5.95E-03
Unclassified	13549	4	5.36	0.75	-	0.00E+00
<i>vtgI</i>-KO Experiment: proteins up-regulated in <i>vtgI</i>-KO eggs (<i>vtgI</i>-KO; N=94, ≥ 4 samples >1.5 fold)						
Analysis Type: PANTHER Overrepresentation Test (Released 20190711)						
Annotation Version and Release Date: PANTHER version 14.1 Released 2019-03-12						
Reference: Danio rerio						
Test Type: Fisher's Exact						
Correction: Bonferroni correction for multiple testing ($p < 0.05$)						
<i>PANTHER GO-Slim Biological Process</i>	#REF	#Protein	Expected	Fold	+/-	P value
Cellular response to heat	22	3	0.03	98.53	+	0.00766
Response to heat	22	3	0.03	98.53	+	0.00766
Cellular response to unfolded protein	26	3	0.04	83.37	+	0.0121
Response to topologically incorrect protein	41	3	0.06	52.87	+	0.0433
Response to unfolded protein	26	3	0.04	83.37	+	0.0121
Chaperone-mediated protein folding	32	3	0.04	67.74	+	0.0216
Exocytosis	77	5	0.11	46.92	+	0.000133
Vesicle-mediated transport	705	8	0.98	8.2	+	0.00641
Cytokinesis	97	5	0.13	37.24	+	0.000398
Cell division	100	5	0.14	36.13	+	0.000461
Anatomical structure morphogenesis	198	5	0.27	18.25	+	0.0118
Unclassified	12906	8	17.86	0.45	-	0
<i>PANTHER GO-Slim Molecular Function</i>	#REF	#Protein	Expected	Fold	+/-	P value
Heat shock protein binding	28	3	0.04	77.42	+	0.0048
Ubiquitin protein ligase binding	35	3	0.05	61.93	+	0.00894
ATP binding	47	3	0.07	46.12	+	0.0205
Purine ribonucleotide binding	63	3	0.09	34.41	+	0.0472
Nucleotide binding	141	4	0.2	20.5	+	0.0213
Unfolded protein binding	59	3	0.08	36.74	+	0.0392
Structural molecule activity	565	7	0.78	8.95	+	0.00509
Unclassified	13549	6	18.75	0.32	-	0
<i>PANTHER GO-Slim Cellular Component</i>	#REF	#Protein	Expected	Fold	+/-	P value
Actin cytoskeleton	301	5	0.42	12	+	0.0228
Cytosol	724	7	1	6.99	+	0.0204
Unclassified	13836	16	19.15	0.84	-	0
<i>PANTHER Protein Class</i>	#REF	#Protein	Expected	Fold	+/-	P value

Actin and actin related protein	26	5	0.04	> 100	+	0.00000012
Actin family cytoskeletal protein	298	5	0.41	12.12	+	0.0117
Translation elongation factor	38	3	0.05	57.04	+	0.00507
RNA binding protein	628	6	0.87	6.9	+	0.0429
Translation initiation factor	77	3	0.11	28.15	+	0.0377
Dehydrogenase	205	4	0.28	14.1	+	0.0394
Unclassified	14588	13	20.19	0.64	-	0
<i>PANTHER Pathways</i>						
Cytoskeletal regulation by Rho GTPase	98	5	0.14	36.86	+	0.0000458
Nicotinic acetylcholine receptor signaling pathway	121	5	0.17	29.86	+	0.000125
Cadherin signaling pathway	142	5	0.2	25.44	+	0.000267
Alzheimer disease-presenilin pathway	148	5	0.2	24.41	+	0.000326
Huntington disease	187	6	0.26	23.18	+	0.0000377
Inflammation mediated by chemokine and cytokine signaling pathway	298	5	0.41	12.12	+	0.00884
Wnt signaling pathway	332	5	0.46	10.88	+	0.0146
Unclassified	22310	23	30.88	0.74	-	0

Table S4. Complete PANTHER Overrepresentation analysis for differentially regulated proteins in the *vtg3*-KO experiment

<i>vtg3</i>-KO Experiment: proteins down-regulated in <i>vtg3</i>-KO eggs (Wt; N=21 $\geq$4 samples >1.5 fold)						
Analysis Type: PANTHER Overrepresentation Test (Released 20190711)						
Annotation Version and Release Date: PANTHER version 14.1 Released 2019-03-12						
Test Type: Fisher's Exact						
Reference: Danio rerio						
Correction: Bonferroni correction for multiple testing ($p < 0.05$)						
<i>PANTHER GO-Slim Biological Process (uncorrected)</i>	#REF	#Protein	Expected	Fold	+/-	P value
Carbohydrate metabolic process	204	1	0.05	20.66	+	4.77E-02
Monosaccharide metabolic process	87	1	0.02	48.45	+	2.07E-02
Response to organic cyclic compound	34	1	0.01	> 100	+	8.27E-03
Response to estradiol	23	1	0.01	> 100	+	5.68E-03
<i>PANTHER GO-Slim Molecular Function</i>	#REF	#Protein	Expected	Fold	+/-	P value
Phosphatidylinositol-3-phosphate binding	13	2	0	> 100	+	2.23E-03
Phosphatidylinositol phosphate binding	40	2	0.01	> 100	+	1.82E-02
Unclassified	13549	1	3.21	0.31	-	0.00E+00
<i>PANTHER GO-Slim Cellular Component</i>	#REF	#Protein	Expected	Fold	+/-	P value
Autophagosome	30	2	0.01	> 100	+	8.79E-03
Lysosomal membrane	33	2	0.01	> 100	+	1.05E-02
Unclassified	13836	4	3.28	1.22	+	0.00E+00
<i>vtg3</i>-KO Experiment: proteins up-regulated in <i>vtg3</i>-KO eggs (<i>vtg3</i>-KO; N=53 $\geq$4 samples >1.5 fold)						
Analysis Type: PANTHER Overrepresentation Test (Released 20190711)						
Annotation Version and Release Date: PANTHER version 14.1 Released 2019-03-12						
Test Type: Fisher's Exact						
Reference: Danio rerio						
Correction: Bonferroni correction for multiple testing ($p < 0.05$)						
<i>PANTHER GO-Slim Biological Process</i>	#REF	#Protein	Expected	Fold	+/-	P value
Cellular response to heat	22	5	0.03	> 100	+	1.83E-07
Response to heat	22	5	0.03	> 100	+	1.83E-07
Cellular response to unfolded protein	26	5	0.03	> 100	+	3.85E-07
Response to topologically incorrect protein	41	5	0.05	> 100	+	3.07E-06
Response to unfolded protein	26	5	0.03	> 100	+	3.85E-07
Chaperone-mediated protein folding	32	5	0.04	> 100	+	9.82E-07
Protein folding	123	6	0.15	41.12	+	1.18E-05
Exocytosis	77	6	0.09	65.69	+	8.10E-07
Vesicle-mediated transport	705	11	0.84	13.15	+	4.04E-07
Transport	1403	12	1.66	7.21	+	4.21E-05
Establishment of localization	1403	12	1.66	7.21	+	4.21E-05
Localization	2306	13	2.74	4.75	+	1.17E-03
Cytokinesis	97	6	0.12	52.14	+	3.02E-06
Cell division	100	6	0.12	50.58	+	3.59E-06

Modification-dependent protein catabolic process	81	4	0.1	41.63	+	4.27E-03
Anatomical structure morphogenesis	198	7	0.23	29.8	+	5.04E-06
Anatomical structure development	400	7	0.47	14.75	+	5.48E-04
Developmental process	569	7	0.67	10.37	+	5.53E-03
Endocytosis	326	6	0.39	15.51	+	3.11E-03
Unclassified	12906	6	15.31	0.39	-	0.00E+00
<i>PANTHER GO-Slim Molecular Function</i>						
Heat shock protein binding	28	5	0.03	> 100	+	1.73E-07
Ubiquitin protein ligase binding	35	4	0.04	96.34	+	5.80E-05
ATP binding	47	5	0.06	89.68	+	1.86E-06
Purine ribonucleotide binding	63	5	0.07	66.9	+	7.37E-06
Ribonucleotide binding	70	5	0.08	60.21	+	1.21E-05
Nucleotide binding	141	5	0.17	29.89	+	3.42E-04
Small molecule binding	300	5	0.36	14.05	+	1.24E-02
Unfolded protein binding	59	5	0.07	71.44	+	5.41E-06
ATPase activity, coupled	244	5	0.29	17.27	+	4.67E-03
ATPase activity	312	5	0.37	13.51	+	1.49E-02
Structural molecule activity	565	9	0.67	13.43	+	6.30E-06
Unclassified	13549	3	16.07	0.19	-	0.00E+00
<i>PANTHER GO-Slim Cellular Component</i>						
Actin cytoskeleton	301	6	0.36	16.8	+	5.33E-04
Organelle	4516	16	5.36	2.99	+	4.62E-03
Cytosol	724	8	0.86	9.31	+	5.93E-04
Unclassified	13836	11	16.41	0.67	-	0.00E+00
<i>PANTHER Protein Class</i>						
Amino acid kinase	8	3	0.01	> 100	+	5.02E-05
Actin and actin related protein	26	6	0.03	> 100	+	2.94E-10
Actin family cytoskeletal protein	298	6	0.35	16.97	+	2.71E-04
Cytoskeletal protein	620	6	0.74	8.16	+	1.63E-02
Ribosomal protein	146	4	0.17	23.09	+	5.87E-03
Unclassified	14588	13	17.31	0.75	-	0.00E+00
<i>PANTHER Pathways</i>						
Cytoskeletal regulation by Rho GTPase	98	6	0.12	51.61	+	3.50E-07
Nicotinic acetylcholine receptor signaling pathway	121	6	0.14	41.8	+	1.17E-06
Parkinson disease	110	5	0.13	38.32	+	3.55E-05
Cadherin signaling pathway	142	6	0.17	35.62	+	2.93E-06
Alzheimer disease-presenilin pathway	148	6	0.18	34.17	+	3.72E-06
Huntington disease	187	6	0.22	27.05	+	1.43E-05
Apoptosis signaling pathway	161	5	0.19	26.18	+	2.19E-04
Inflammation mediated by chemokine and cytokine signaling pathway	298	6	0.35	16.97	+	2.05E-04
Wnt signaling pathway	332	6	0.39	15.23	+	3.78E-04
Unclassified	22310	18	26.47	0.68	-	0.00E+00

Table S5. Complete network enrichment analyses for differentially regulated proteins which were resolved in a STRING subnetwork in the *vtgI*-KO Experiment. **A)** proteins down-regulated in *vtgI*-KO eggs. **B)** proteins up-regulated in *vtgI*-KO eggs. Only statistically significant results are reported (χ^2 , $p < 0.05$).

A) <i>vtgI</i>-KO Experiment: Network stats for proteins down-regulated in <i>vtgI</i>-KO eggs (Wt; N=32)			
number of nodes:	17		
number of edges:	18		
average node degree:	2.12		
clustering coefficient:	0.64		
expected number of edges:	6		
PPI enrichment p-value:	2.75E-05		
confidence level:	0.15		
<i>KEGG Pathways</i>			
pathway	description	protein count	FDR
<u>dre00330</u>	Arginine and proline metabolism	2 of 58	0.0074
<i>Reactome Pathways</i>			
pathway	description	protein count	FDR
<u>DRE-71288</u>	Creatine metabolism	2 of 10	0.0001
<i>UniProt Keywords</i>			
keyword	description	protein count	FDR
<u>KW-0732</u>	Signal	8 of 3209	0.0075
<i>PFAM Protein Domains</i>			
domain	description	protein count	FDR
<u>PF09175</u>	Domain of unknown function (DUF1944)	3 of 8	8.71E-07
<u>PF09172</u>	Domain of unknown function (DUF1943)	3 of 12	1.20E-06
<u>PF01347</u>	Lipoprotein amino terminal region	3 of 13	1.20E-06
<u>PF02807</u>	ATP:guanido phosphotransferase, N-terminal domain	2 of 7	8.38E-05
<u>PF00217</u>	ATP:guanido phosphotransferase, C-terminal catalytic do.	2 of 7	8.38E-05
<u>PF13347</u>	MFS/sugar transport protein	2 of 14	0.00019
<u>PF00354</u>	Pentaxin family	2 of 25	0.00046
<u>PF13385</u>	Concanavalin A-like lectin/glucanases superfamily	2 of 33	0.00069
<u>PF02140</u>	Galactose binding lectin domain	2 of 48	0.0012
<u>PF07690</u>	Major Facilitator Superfamily	2 of 154	0.0107
<i>INTERPRO Protein Domains and Features</i>			
domain	description	protein count	FDR
<u>IPR037088</u>	Vitellinogen, beta-sheet shell domain superfamily	3 of 8	1.56E-06
<u>IPR015819</u>	Lipid transport protein, beta-sheet shell	3 of 13	1.56E-06
<u>IPR015817</u>	Vitellinogen, open beta-sheet, subdomain 1	3 of 9	1.56E-06
<u>IPR015816</u>	Vitellinogen, beta-sheet N-terminal	3 of 12	1.56E-06
<u>IPR015258</u>	Vitellinogen, beta-sheet shell	3 of 8	1.56E-06
<u>IPR015255</u>	Vitellinogen, open beta-sheet	3 of 12	1.56E-06
<u>IPR011030</u>	Lipovitellin-phosvitin complex, superhelical domain	3 of 13	1.56E-06
<u>IPR001747</u>	Lipid transport protein, N-terminal	3 of 13	1.56E-06
<u>IPR001759</u>	Pentraxin-related	2 of 21	0.00047
<u>IPR000922</u>	D-galactoside/L-rhamnose binding SUEL lectin domain	2 of 38	0.0013
<u>IPR020846</u>	Major facilitator superfamily domain	2 of 148	0.0161
<u>IPR036259</u>	MFS transporter superfamily	2 of 177	0.0208
<i>SMART Protein Domains</i>			
domain	description	protein count	FDR
<u>SM01170</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	3 of 8	2.90E-07
<u>SM01169</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	3 of 12	4.00E-07
<u>SM00638</u>	Lipoprotein N-terminal Domain	3 of 12	4.00E-07
B) <i>vtgI</i>-KO Experiment: Network stats for proteins up-regulated in <i>vtgI</i>-KO eggs (<i>vtgI</i>-KO; N=94)			
number of nodes:	63		
number of edges:	107		
average node degree:	3.4		
clustering coefficient:	0.387		
expected number of edges:	58		
PPI enrichment p-value:	5.95E-09		
confidence level:	0.40		
<i>KEGG Pathways</i>			
pathway	description	protein count	FDR

dre00270	Cysteine and methionine metabolism	3 of 47	0.0072
dre04260	Cardiac muscle contraction	3 of 89	0.0135
dre04141	Protein processing in endoplasmic reticulum	4 of 176	0.0135
dre01100	Metabolic pathways	10 of 1278	0.0135
dre00790	Folate biosynthesis	2 of 26	0.0135
dre00620	Pyruvate metabolism	2 of 41	0.0244
dre03013	RNA transport	3 of 151	0.0263
dre04261	Adrenergic signaling in cardiomyocytes	3 of 180	0.0368
dre00983	Drug metabolism - other enzymes	2 of 61	0.0368
dre00010	Glycolysis / Gluconeogenesis	2 of 74	0.0439

Reactome Pathways

pathway	description	protein count	FDR
DRE-71182	Phenylalanine and tyrosine catabolism	3 of 14	0.003
DRE-450408	AUF1 (hnRNP D0) binds and destabilizes mRNA	4 of 54	0.003
DRE-3371568	Attenuation phase	3 of 19	0.003
DRE-3371497	HSP90 chaperone cycle for steroid hormone receptors	3 of 21	0.003
DRE-6798695	Neutrophil degranulation	7 of 490	0.0088
DRE-168256	Immune System	11 of 1379	0.0154
DRE-3371453	Regulation of HSF1-mediated heat shock response	3 of 69	0.0238
DRE-1430728	Metabolism	12 of 1751	0.0258
DRE-2262752	Cellular responses to stress	5 of 321	0.0313
DRE-168249	Innate Immune System	8 of 875	0.0313
DRE-140837	Intrinsic Pathway of Fibrin Clot Formation	2 of 19	0.0313
DRE-140875	Common Pathway of Fibrin Clot Formation	2 of 23	0.0365
DRE-901042	Calnexin/calreticulin cycle	2 of 25	0.0387

UniProt Keywords

keyword	description	protein count	FDR
KW-0547	Nucleotide-binding	16 of 1588	2.80E-05
KW-0251	Elongation factor	3 of 16	0.00018
KW-0067	ATP-binding	13 of 1287	0.00018
KW-0732	Signal	19 of 3209	0.00099
KW-0520	NAD	4 of 98	0.00099
KW-0676	Redox-active center	2 of 24	0.0095
KW-0560	Oxidoreductase	4 of 349	0.0473

PFAM Protein Domains

domain	description	protein count	FDR
PF02140	Galactose binding lectin domain	13 of 48	7.00E-21
PF00022	Actin	8 of 24	1.82E-13
PF06723	MreB/Mbl protein	4 of 17	3.15E-06
PF00012	Hsp70 protein	4 of 19	3.48E-06
PF03143	Elongation factor Tu C-terminal domain	3 of 9	3.11E-05
PF14560	Ubiquitin-like domain	3 of 10	3.37E-05
PF03144	Elongation factor Tu domain 2	3 of 18	0.00013
PF11976	Ubiquitin-2 like Rad60 SUMO-like	3 of 22	0.0002
PF10569	Alpha-macro-globulin thiol-ester bond-forming region	3 of 22	0.0002
PF07703	Alpha-2-macroglobulin family N-terminal region	3 of 23	0.0002
PF07678	A-macroglobulin complement component	3 of 24	0.0002
PF07677	A-macroglobulin receptor	3 of 24	0.0002
PF01835	MG2 domain	3 of 23	0.0002
PF00207	Alpha-2-macroglobulin family	3 of 23	0.0002
PF00009	Elongation factor Tu GTP binding domain	3 of 35	0.00038
PF00056	lactate/malate dehydrogenase, NAD binding domain	2 of 6	0.00054
PF00240	Ubiquitin family	3 of 42	0.00056
PF02866	lactate/malate dehydrogenase, alpha/beta C-terminal do.	2 of 7	0.00062
PF09175	Domain of unknown function (DUF1944)	2 of 8	0.00073
PF09172	Domain of unknown function (DUF1943)	2 of 12	0.0014
PF01347	Lipoprotein amino terminal region	2 of 13	0.0015
PF13848	Thioredoxin-like domain	2 of 14	0.0017
PF00085	Thioredoxin	2 of 33	0.0077
PF00079	Serpin (serine protease inhibitor)	2 of 33	0.0077
PF00059	Lectin C-type domain	3 of 202	0.0289

INTERPRO Protein Domains and Features

domain	description	protein count	FDR
IPR004001	Actin, conserved site	7 of 12	1.65E-12
IPR020902	Actin/actin-like conserved site	7 of 16	3.99E-12
IPR004000	Actin family	7 of 21	1.27E-11
IPR000922	D-galactoside/L-rhamnose binding SUEL lectin domain	6 of 38	2.57E-08
IPR029048	Heat shock protein 70kD, C-terminal domain superf.	4 of 17	3.01E-06
IPR029047	Heat shock protein 70kD, peptide-binding domain superf.	4 of 16	3.01E-06
IPR018181	Heat shock protein 70, conserved site	4 of 16	3.01E-06
IPR013126	Heat shock protein 70 family	4 of 18	3.01E-06

<u>IPR036291</u>	NAD(P)-binding domain superfamily	7 of 203	8.27E-06
<u>IPR004539</u>	Translation elongation factor EF1A, eukaryotic/archaeal	3 of 5	8.27E-06
<u>IPR019956</u>	Ubiquitin	3 of 9	2.78E-05
<u>IPR019954</u>	Ubiquitin conserved site	3 of 9	2.78E-05
<u>IPR004160</u>	Translation elongation factor EFTu/EF1A, C-terminal	3 of 9	2.78E-05
<u>IPR002353</u>	Type-2 ice-structuring protein	3 of 11	3.60E-05
<u>IPR009001</u>	Translation elongation factor EF1A/initiation factor IF2gamma, C-terminal	3 of 13	5.15E-05
<u>IPR031157</u>	Tr-type G domain, conserved site	3 of 15	7.01E-05
<u>IPR019742</u>	Alpha-2-macroglobulin, conserved site	3 of 17	9.19E-05
<u>IPR004161</u>	Translation elongation factor EFTu-like, domain 2	3 of 18	0.0001
<u>IPR002890</u>	Macroglobulin domain	3 of 19	0.00011
<u>IPR036595</u>	Alpha-macroglobulin, receptor-binding domain superf.	3 of 20	0.00012
<u>IPR011626</u>	Alpha-macroglobulin, TED domain	3 of 20	0.00012
<u>IPR011625</u>	Alpha-2-macroglobulin, bait region domain	3 of 20	0.00012
<u>IPR009048</u>	Alpha-macroglobulin, receptor-binding	3 of 20	0.00012
<u>IPR001599</u>	Alpha-2-macroglobulin	3 of 20	0.00012
<u>IPR008930</u>	Terpenoid cyclases/protein prenyltransferase alpha-alpha toroid	3 of 24	0.00016
<u>IPR000795</u>	Transcription factor, GTP-binding domain	3 of 25	0.00017
<u>IPR009000</u>	Translation protein, beta-barrel domain superfamily	3 of 33	0.00035
<u>IPR001236</u>	Lactate/malate dehydrogenase, N-terminal	2 of 6	0.00061
<u>IPR022383</u>	Lactate/malate dehydrogenase, C-terminal	2 of 7	0.00075
<u>IPR015955</u>	Lactate dehydrogenase/glycoside hydrolase, family 4, Ct	2 of 7	0.00075
<u>IPR001557</u>	L-lactate/malate dehydrogenase	2 of 7	0.00075
<u>IPR037088</u>	Vitellinogen, beta-sheet shell domain superfamily	2 of 8	0.00085
<u>IPR015258</u>	Vitellinogen, beta-sheet shell	2 of 8	0.00085
<u>IPR015817</u>	Vitellinogen, open beta-sheet, subdomain 1	2 of 9	0.00098
<u>IPR011332</u>	Zinc-binding ribosomal protein	2 of 9	0.00098
<u>IPR000626</u>	Ubiquitin domain	3 of 58	0.0013
<u>IPR015816</u>	Vitellinogen, beta-sheet N-terminal	2 of 12	0.0015
<u>IPR015255</u>	Vitellinogen, open beta-sheet	2 of 12	0.0015
<u>IPR015819</u>	Lipid transport protein, beta-sheet shell	2 of 13	0.0016
<u>IPR011030</u>	Lipovitellin-phosvitin complex, superhelical domain	2 of 13	0.0016
<u>IPR001747</u>	Lipid transport protein, N-terminal	2 of 13	0.0016
<u>IPR018378</u>	C-type lectin, conserved site	3 of 81	0.0028
<u>IPR014756</u>	Immunoglobulin E-set	3 of 139	0.0119
<u>IPR001304</u>	C-type lectin-like	3 of 138	0.0119
<u>IPR016186</u>	C-type lectin-like/link domain superfamily	3 of 154	0.0153
<u>IPR016187</u>	C-type lectin fold	3 of 163	0.0174
<u>IPR029071</u>	Ubiquitin-like domain superfamily	3 of 204	0.031
<u>IPR016040</u>	NAD(P)-binding domain	2 of 75	0.0333
<u>IPR005225</u>	Small GTP-binding protein domain	3 of 232	0.0416
<i>SMART Protein Domains</i>			
domain	description	protein count	FDR
<u>SM00268</u>	Actin	8 of 24	1.04E-13
<u>SM01361</u>	A-macroglobulin receptor	3 of 24	0.00026
<u>SM01360</u>	Alpha-2-macroglobulin family	3 of 23	0.00026
<u>SM01359</u>	Alpha-2-Macroglobulin	3 of 23	0.00026
<u>SM01170</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	2 of 8	0.0007
<u>SM00213</u>	Ubiquitin homologues	3 of 46	0.0007
<u>SM01169</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	2 of 12	0.0011
<u>SM00638</u>	Lipoprotein N-terminal Domain	2 of 12	0.0011
<u>SM00093</u>	SERine Proteinase INHibitors	2 of 31	0.005
<u>SM00034</u>	C-type lectin (CTL) or carbohydrate-recognition domain	3 of 202	0.0207

Table S6. Complete network enrichment analyses for differentially regulated proteins which were resolved in a STRING subnetwork in the *vtg3*-KO Experiment. **A)** proteins down-regulated in *vtg3*-KO eggs. **B)** proteins up-regulated in *vtg3*-KO eggs. Only statistically significant results are reported (χ^2 , $p < 0.05$).

A) <i>vtg3</i>-KO Experiment: Network stats for proteins down-regulated in <i>vtg3</i>-KO eggs (Wt; N=21)			
number of nodes:	11		
number of edges:	7		
average node degree:	1.27		
clustering coefficient:	0.394		
expected number of edges:	1		
PPI enrichment p-value:	6.99E-06		
confidence level:	0.4		
<i>KEGG Pathways</i>			
pathway	description	protein counts	FDR
<u>dre01200</u>	Carbon metabolism	2 of 125	0.0147
<i>PFAM Protein Domains</i>			
domain	description	protein counts	FDR
<u>PF06462</u>	Propeller	2 of 7	9.62E-05
<u>PF13347</u>	MFS/sugar transport protein	2 of 14	0.00016
<u>PF07690</u>	Major Facilitator Superfamily	2 of 154	0.0104
<i>INTERPRO Protein Domains and Features</i>			
domain	description	protein counts	FDR
<u>IPR006624</u>	Beta-propeller repeat TECPR	2 of 7	0.0002
<u>IPR036259</u>	MFS transporter superfamily	2 of 177	0.0298
<u>IPR020846</u>	Major facilitator superfamily domain	2 of 148	0.0298
<i>SMART Protein Domains</i>			
domain	description	protein counts	FDR
<u>SM00706</u>	Beta propeller repeats in Physarum polycephalum tectonins, Limulus lectin L-6 and animal hypothetical proteins.	2 of 8	4.24E-05
B) <i>vtg3</i>-KO Experiment: Network stats for proteins up-regulated in <i>vtg3</i>-KO eggs (<i>vtg3</i>-KO; N=53)			
number of nodes:	36		
number of edges:	46		
average node degree:	2.56		
clustering coefficient:	0.417		
expected number of edges:	36		
PPI enrichment p-value:	0.0517		
confidence level:	0.4		
<i>KEGG Pathways</i>			
pathway	description	protein count	FDR
<u>dre04141</u>	Protein processing in endoplasmic reticulum	6 of 176	3.04E-06
<u>dre00270</u>	Cysteine and methionine metabolism	4 of 47	6.54E-06
<u>dre00620</u>	Pyruvate metabolism	3 of 41	0.00019
<u>dre00330</u>	Arginine and proline metabolism	3 of 58	0.00037
<u>dre04260</u>	Cardiac muscle contraction	3 of 89	0.001
<u>dre01100</u>	Metabolic pathways	8 of 1278	0.001
<u>dre03040</u>	Spliceosome	3 of 131	0.0022
<u>dre00640</u>	Propanoate metabolism	2 of 31	0.0022
<u>dre04261</u>	Adrenergic signaling in cardiomyocytes	3 of 180	0.0041
<u>dre00010</u>	Glycolysis / Gluconeogenesis	2 of 74	0.0091
<u>dre04144</u>	Endocytosis	3 of 293	0.013
<u>dre04010</u>	MAPK signaling pathway	3 of 359	0.0206
<u>dre03010</u>	Ribosome	2 of 126	0.0206
<i>Reactome Pathways</i>			
pathway	description	protein count	FDR
<u>DRE-450408</u>	AUF1 (hnRNP D0) binds and destabilizes mRNA	5 of 54	5.35E-06
<u>DRE-3371568</u>	Attenuation phase	4 of 19	5.35E-06
<u>DRE-3371497</u>	HSP90 chaperone cycle for steroid hormone receptors (SHR)	4 of 21	5.35E-06
<u>DRE-71288</u>	Creatine metabolism	3 of 10	3.53E-05
<u>DRE-3371453</u>	Regulation of HSF1-mediated heat shock response	4 of 69	0.00014
<u>DRE-2262752</u>	Cellular responses to stress	6 of 321	0.0002
<u>DRE-71406</u>	Pyruvate metabolism and Citric Acid (TCA) cycle	3 of 55	0.002
<u>DRE-189085</u>	Digestion of dietary carbohydrate	2 of 11	0.0037
<u>DRE-71291</u>	Metabolism of amino acids and derivatives	4 of 249	0.0076
<u>DRE-901042</u>	Calnexin/calreticulin cycle	2 of 25	0.0111
<u>DRE-70268</u>	Pyruvate metabolism	2 of 31	0.0157
<u>DRE-168256</u>	Immune System	7 of 1379	0.0343

DRE-390522	Striated Muscle Contraction	2 of 54	0.0372
DRE-5358346	Hedgehog ligand biogenesis	2 of 58	0.0408

UniProt Keywords

keyword	description	protien count	FDR
KW-0067	ATP-binding	15 of 1287	1.07E-09
KW-0676	Redox-active center	3 of 24	5.07E-05
KW-0520	NAD	4 of 98	6.41E-05
KW-0413	Isomerase	3 of 81	0.00094
KW-0560	Oxidoreductase	3 of 349	0.0462

PFAM Protein Domains

domain	description	protien count	FDR
PF00022	Actin	8 of 24	1.62E-15
PF06723	MreB/Mbl protein	5 of 17	1.40E-09
PF00012	Hsp70 protein	5 of 19	1.50E-09
PF00056	lactate/malate dehydrogenase, NAD binding do.	3 of 6	1.50E-06
PF02866	lactate/malate dehydrogenase, alpha/beta C-terminal domain	3 of 7	1.71E-06
PF02807	ATP:guanido phosphotransferase, N-terminal do.	3 of 7	1.71E-06
PF00217	ATP:guanido phosphotransferase, C-terminal catalytic domain	3 of 7	1.71E-06
PF14560	Ubiquitin-like domain	3 of 10	2.54E-06
PF13848	Thioredoxin-like domain	3 of 14	5.35E-06
PF11976	Ubiquitin-2 like Rad60 SUMO-like	3 of 22	1.62E-05
PF00085	Thioredoxin	3 of 33	4.51E-05
PF00240	Ubiquitin family	3 of 42	8.15E-05
PF02140	Galactose binding lectin domain	3 of 48	0.00011
PF01216	Calsequestrin	2 of 7	0.00014
PF09175	Domain of unknown function (DUF1944)	2 of 8	0.00017
PF09172	Domain of unknown function (DUF1943)	2 of 12	0.00031
PF01347	Lipoprotein amino terminal region	2 of 13	0.00034

INTERPRO Protein Domains and Features

domain	description	protein count	FDR
IPR004001	Actin, conserved site	7 of 12	1.41E-14
IPR020902	Actin/actin-like conserved site	7 of 16	3.41E-14
IPR004000	Actin family	7 of 21	1.09E-13
IPR029048	Heat shock protein 70kD, C-terminal domain superf.	5 of 17	1.07E-09
IPR029047	Heat shock protein 70kD, peptide-binding domain superf.	5 of 16	1.07E-09
IPR018181	Heat shock protein 70, conserved site	5 of 16	1.07E-09
IPR013126	Heat shock protein 70 family	5 of 18	1.07E-09
IPR001236	Lactate/malate dehydrogenase, N-terminal	3 of 6	1.47E-06
IPR022383	Lactate/malate dehydrogenase, C-terminal	3 of 7	1.87E-06
IPR015955	Lactate dehydrogenase/glycoside hydrolase, family 4, C-terminal	3 of 7	1.87E-06
IPR001557	L-lactate/malate dehydrogenase	3 of 7	1.87E-06
IPR019956	Ubiquitin	3 of 9	2.56E-06
IPR019954	Ubiquitin conserved site	3 of 9	2.56E-06
IPR018177	L-lactate dehydrogenase, active site	2 of 3	7.82E-05
IPR011304	L-lactate dehydrogenase	2 of 3	7.82E-05
IPR000922	D-galactoside/L-rhamnose binding SUEL lectin do.	3 of 38	9.07E-05
IPR005792	Protein disulphide isomerase	2 of 5	0.00014
IPR036802	ATP:guanido phosphotransferase, N-terminal do. Superf.	2 of 6	0.00017
IPR022415	ATP:guanido phosphotransferase active site	2 of 6	0.00017
IPR022414	ATP:guanido phosphotransferase, catalytic domain	2 of 6	0.00017
IPR022413	ATP:guanido phosphotransferase, N-terminal	2 of 6	0.00017
IPR005788	Disulphide isomerase	2 of 7	0.00017
IPR000749	ATP:guanido phosphotransferase	2 of 6	0.00017
IPR037088	Vitellinogen, beta-sheet shell domain superfamily	2 of 8	0.0002
IPR015258	Vitellinogen, beta-sheet shell	2 of 8	0.0002
IPR000626	Ubiquitin domain	3 of 58	0.0002
IPR015817	Vitellinogen, open beta-sheet, subdomain 1	2 of 9	0.00022
IPR011332	Zinc-binding ribosomal protein	2 of 9	0.00022
IPR036291	NAD(P)-binding domain superfamily	4 of 203	0.00034
IPR016040	NAD(P)-binding domain	3 of 75	0.00034
IPR015819	Lipid transport protein, beta-sheet shell	2 of 13	0.00034
IPR015816	Vitellinogen, beta-sheet N-terminal	2 of 12	0.00034
IPR015255	Vitellinogen, open beta-sheet	2 of 12	0.00034
IPR014746	Glutamine synthetase/guanido kinase, catalytic do.	2 of 12	0.00034
IPR011030	Lipovitellin-phosvitin complex, superhelical do.	2 of 13	0.00034
IPR001747	Lipid transport protein, N-terminal	2 of 13	0.00034
IPR017937	Thioredoxin, conserved site	2 of 17	0.0005
IPR013766	Thioredoxin domain	2 of 40	0.0024
IPR029071	Ubiquitin-like domain superfamily	3 of 204	0.0044
IPR017853	Glycoside hydrolase superfamily	2 of 62	0.0052
IPR036249	Thioredoxin-like superfamily	2 of 127	0.0198

<i>SMART Protein Domains</i>			
domain	description	protein count	FDR
<u>SM00268</u>	Actin	8 of 24	5.75E-16
<u>SM00213</u>	Ubiquitin homologues	3 of 46	0.00022
<u>SM01170</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	2 of 8	0.00029
<u>SM01169</u>	Members of this family adopt a structure consisting of several large open beta-sheets. Their exact function has not, as yet, been determined [PUBMED:12135361].	2 of 12	0.00045
<u>SM00638</u>	Lipoprotein N-terminal Domain	2 of 12	0.00045