SUPPLEMENTALS

Fig S1. Classifying phenotypic defects in *alms1*$^{-/-}$ zebrafish.

A) Zebrafish *alms1* gene expression in adult fish of indicated genotype. Statistics, One-Way ANOVA. (B) Quantification of cardiac edema over time in *alms1*$^{+/+}$ (n=30) and *alms1*$^{-/-}$ (n=69) larvae. Note the lack of change in percentage over time. (C) Thickness of overall retinal tissue and photoreceptor layer in 6-month-old adult *alms1*$^{+/+}$ (n=4) and *alms1*$^{-/-}$ (n=4) animals. Statistics, One-Way ANOVA. (D) Total fat consumed as assessed by fluorescence per 20 larvae in *alms1*$^{+/+}$ (n=6) and *alms1*$^{-/-}$ (n=7) larvae at 7 dpf. (E) cDNA levels of Alms1 in cultured MIN6 β-cells in control and si-*Alms1* conditions. Statistics, two-tailed Student's t-test with Welch's Correction. Where indicated, ** p <0.01, **** p<0.0001, NS not significant.

Fig S2. ConsensusPath DB analysis of down-regulated and up-regulated genes in *alms1*$^{-/-}$ β-cell enriched populations.

Nodes particular interest from down-regulated (A) and up-regulated (B) genes found to be differentially expressed genes between β-cells isolated from *alms1*$^{+/+}$ and *alms1*$^{-/-}$ zebrafish. Green highlight in B, pancreatic secretion and diabetes-related pathway nodes. (C) Legend indicating scale of pathway components in A and B.

Table S1. Over-abundant Up-regulated Genes in *alms1*$^{-/-}$ β-cell enriched populations as identified by Gene Ontology analysis. All categories significantly enriched over 3-fold are shown. Gene Ontology defined biological process, fold enrichment and p-value.

Table S2. Over-abundant Down-regulated Genes in *alms1*$^{-/-}$ β-cell enriched populations as identified by Gene Ontology analysis. All categories significantly enriched over 3-fold are shown. Gene Ontology defined biological process, fold enrichment and p-value.

FIG S1.

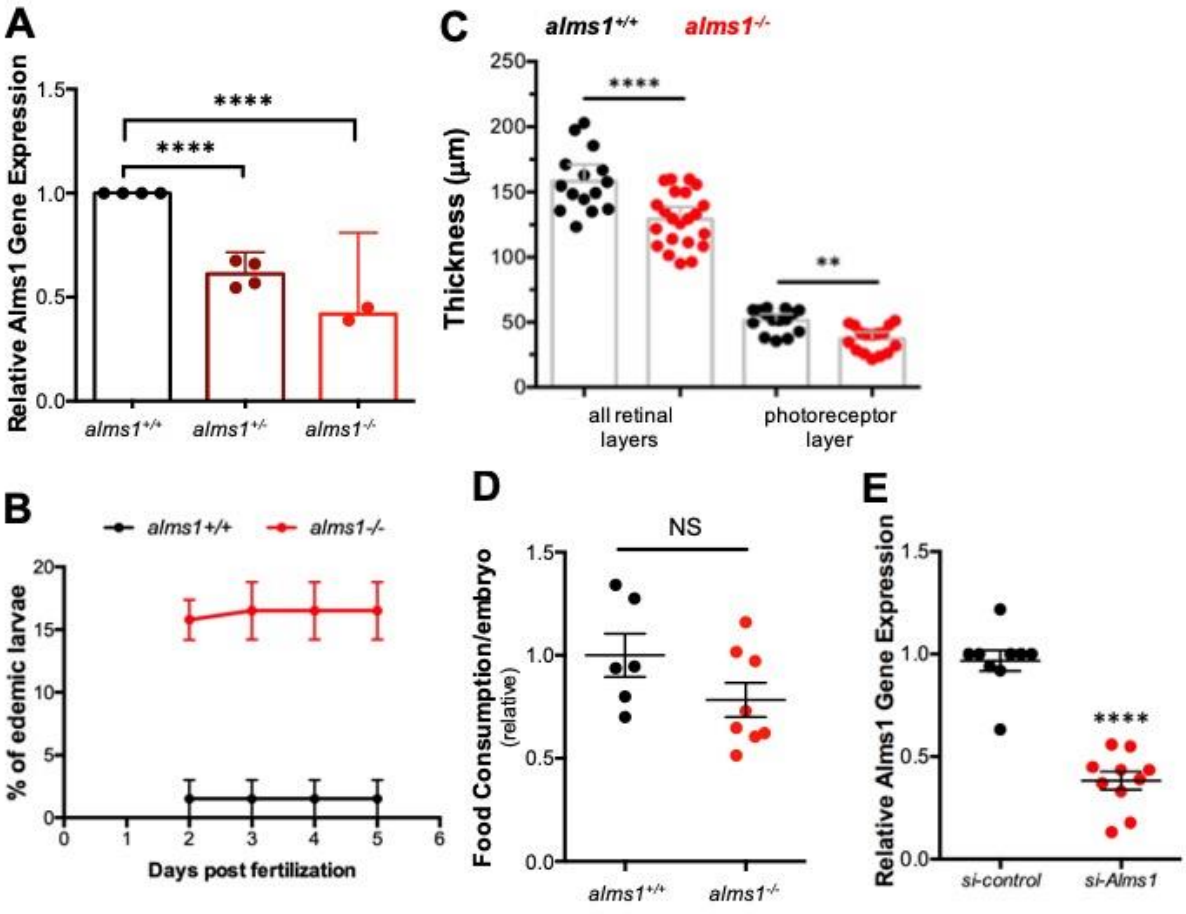
A
Relative Alms1 Gene Expression
1.5
1.0
0.5
0.0
****
****
alms1+/+
alms1+/-
alms1-/-
B
alms1+/+
alms1-/-
% of edemic larvae
20
15
10
5
0
0
1
2
3
4
5
6
Days post fertilization
C
alms1+/+
alms1-/-
Thickness (µm)
250
200
150
100
50
0
****
**
all retinal layers
photoreceptor layer
D
NS
Food Consumption/embryo (relative)
1.5
1.0
0.5
0.0
alms1+/+
alms1-/-
E
Relative Alms1 Gene Expression
1.5
1.0
0.5
0.0
****
si-control
si-Alms1

FIG S2.

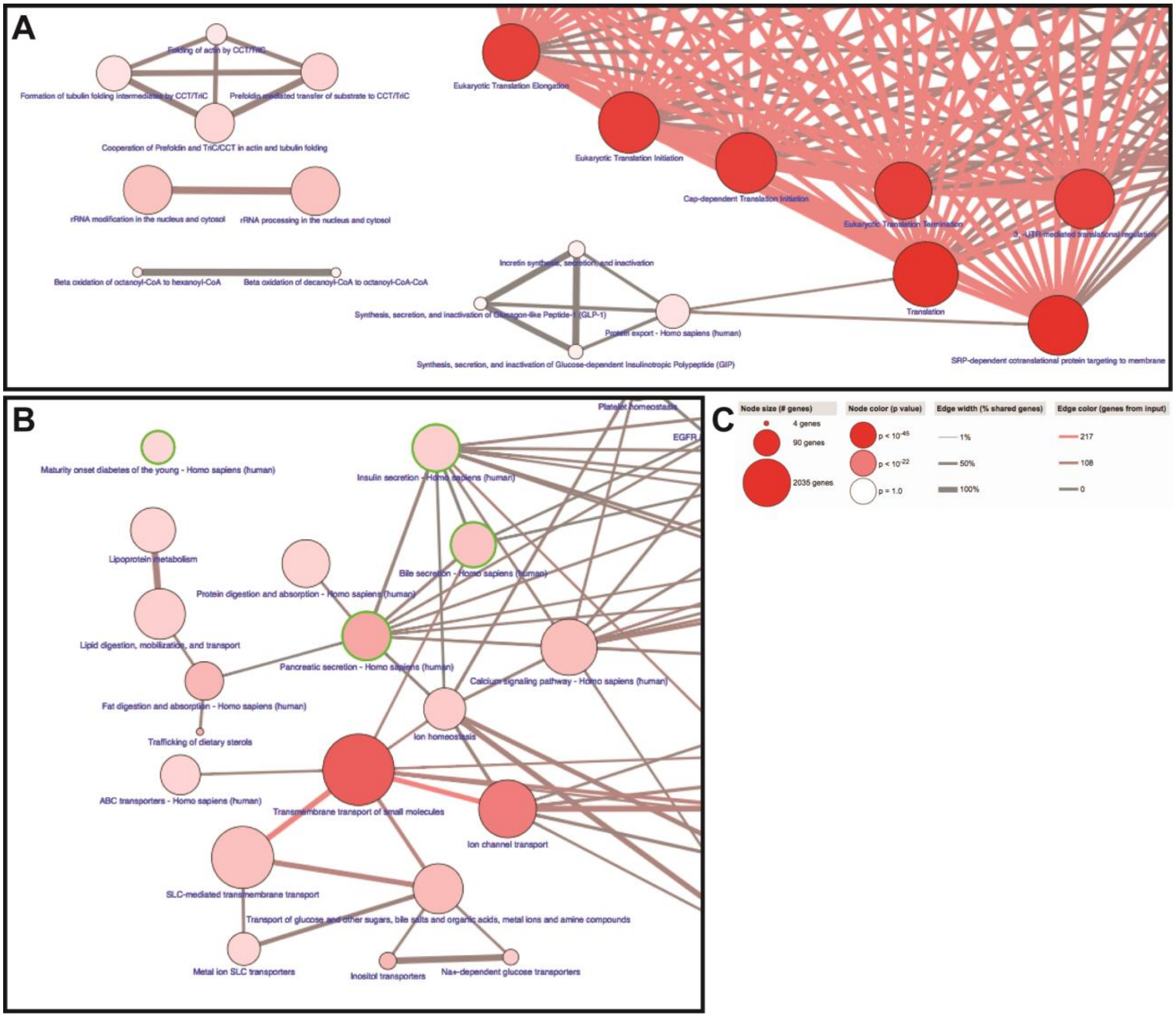
A
Folding of actin by CCT/TriC
Formation of tubulin folding intermediates by CCT/TriC
Prefoldin mediated transfer of substrate to CCT/TriC
Cooperation of Prefoldin and TriC/CCT in actin and tubulin folding
rRNA modification in the nucleus and cytosol
rRNA processing in the nucleus and cytosol
Beta oxidation of octanoyl-CoA to hexanoyl-CoA
Beta oxidation of decanoyl-CoA to octanoyl-CoA-CoA
Eukaryotic Translation Elongation
Eukaryotic Translation Initiation
Cap-dependent Translation Initiation
Eukaryotic Translation Termination
3' -UTR-mediated translational regulation
Translation
SRP-dependent cotranslational protein targeting to membrane
Incretin synthesis, secretion, and inactivation
Synthesis, secretion, and inactivation of Glucagon-like Peptide-1 (GLP-1)
Protein export - Homo sapiens (human)
Synthesis, secretion, and inactivation of Glucose-dependent Insulinotropic Polypeptide (GIP)
B
Platelet homeostasis
EGFR
Maturity onset diabetes of the young - Homo sapiens (human)
Insulin secretion - Homo sapiens (human)
Lipoprotein metabolism
Bile secretion - Homo sapiens (human)
Protein digestion and absorption - Homo sapiens (human)
Lipid digestion, mobilization, and transport
Pancreatic secretion - Homo sapiens (human)
Calcium signaling pathway - Homo sapiens (human)
Fat digestion and absorption - Homo sapiens (human)
Trafficking of dietary sterols
Ion homeostasis
ABC transporters - Homo sapiens (human)
Transmembrane transport of small molecules
Ion channel transport
SLC-mediated transmembrane transport
Transport of glucose and other sugars, bile salts and organic acids, metal ions and amine compounds
Metal ion SLC transporters
Inositol transporters
Na+-dependent glucose transporters
C
Node size (# genes)
4 genes
90 genes
2035 genes
Node color (p value)
p < 10^-45
p < 10^-22
p = 1.0
Edge width (% shared genes)
1%
50%
100%
Edge color (genes from input)
217
108
0

Table S1.

GO Biological Process	Fold Enrichment	P-value
striated muscle myosin thick filament assembly	9.68	6.75E-06
myosin filament assembly	9.68	6.75E-06
myosin filament organization	9.68	6.75E-06
membrane depolarization	7.33	5.09E-06
membrane depolarization during action potential	7.33	5.09E-06
response to alkaloid	7.15	2.27E-05
action potential	6.98	3.26E-06
adenylate cyclase-inhibiting G-protein coupled receptor signaling pathway	5.77	1.34E-04
regulation of cation channel activity	5.44	2.94E-04
calcium ion transmembrane transport	5.35	1.87E-13
calcium ion transport	5.18	9.93E-17
regulation of membrane potential	5.18	5.53E-13
sarcomere organization	4.7	4.44E-03
sensory perception of mechanical stimulus	4.7	4.44E-03
regulation of calcium ion-dependent exocytosis	4.7	4.44E-03
regulation of ion transmembrane transporter activity	4.54	3.16E-03
striated muscle contraction	4.51	1.59E-02
calcium ion-regulated exocytosis of neurotransmitter	4.42	4.13E-02
divalent metal ion transport	4.41	6.46E-15
divalent inorganic cation transport	4.41	6.46E-15
regulation of exocytosis	4.31	1.61E-04
multicellular organismal signaling	4.28	2.84E-02
regulation of transmembrane transporter activity	4.23	7.55E-03
chloride transport	4.12	2.65E-03
regulation of ion transmembrane transport	4.11	3.55E-12
regulation of regulated secretory pathway	4.06	2.52E-02
regulation of transmembrane transport	4.03	7.78E-12
regulation of transporter activity	3.97	1.68E-02
inorganic anion transport	3.91	2.13E-04
detection of abiotic stimulus	3.91	7.93E-04
detection of external stimulus	3.91	7.93E-04
regulation of cation transmembrane transport	3.89	2.17E-02
potassium ion transport	3.89	1.01E-10
regulation of ion transport	3.79	3.76E-11
metal ion transport	3.57	7.65E-26
calcium ion regulated exocytosis	3.51	2.32E-02
cellular component assembly involved in morphogenesis	3.49	8.82E-04
cation transmembrane transport	3.38	2.14E-16

myofibril assembly	3.36	4.90E-03
signal release	3.33	9.36E-03
regulation of secretion by cell	3.27	1.58E-03
ion transmembrane transport	3.19	3.32E-18
adenylate cyclase-modulating G-protein coupled receptor signaling pathway	3.16	1.79E-03
potassium ion transmembrane transport	3.15	8.28E-03
cellular potassium ion transport	3.15	8.28E-03
inorganic cation transmembrane transport	3.13	1.37E-11
cation transport	3.11	9.43E-26
inorganic ion transmembrane transport	3.09	3.94E-12
ion transport	3.08	1.52E-43
regulation of secretion	3.07	4.85E-03

Table S2.

GO Biological Process	Fold Enrichment	P-value
cytoplasmic translation	4.32	4.47E-06
maturation of LSU-rRNA	4.23	7.85E-03
ribosomal large subunit biogenesis	4.15	2.08E-08
ribosome assembly	3.77	2.27E-04
mitochondrial ATP synthesis coupled electron transport	3.55	2.06E-03
translational initiation	3.53	4.93E-07
ribosomal small subunit biogenesis	3.43	9.31E-06
ribonucleoprotein complex assembly	3.37	4.02E-13
ATP synthesis coupled electron transport	3.34	3.21E-03
ribosome biogenesis	3.32	1.14E-20
translation	3.3	2.45E-35
ribonucleoprotein complex biogenesis	3.27	5.29E-29
oxidative phosphorylation	3.26	4.82E-03
peptide biosynthetic process	3.26	1.21E-34
maturation of SSU-rRNA	3.18	7.14E-03
rRNA processing	3.17	4.20E-12
rRNA metabolic process	3.14	3.35E-13
ribonucleoprotein complex subunit organization	3.12	1.35E-11
amide biosynthetic process	3.02	4.93E-32