Appendix

Concerted regulation of mitochondrial and nuclear non-coding RNAs by a dual-targeted RNase Z

Siira *et al.*

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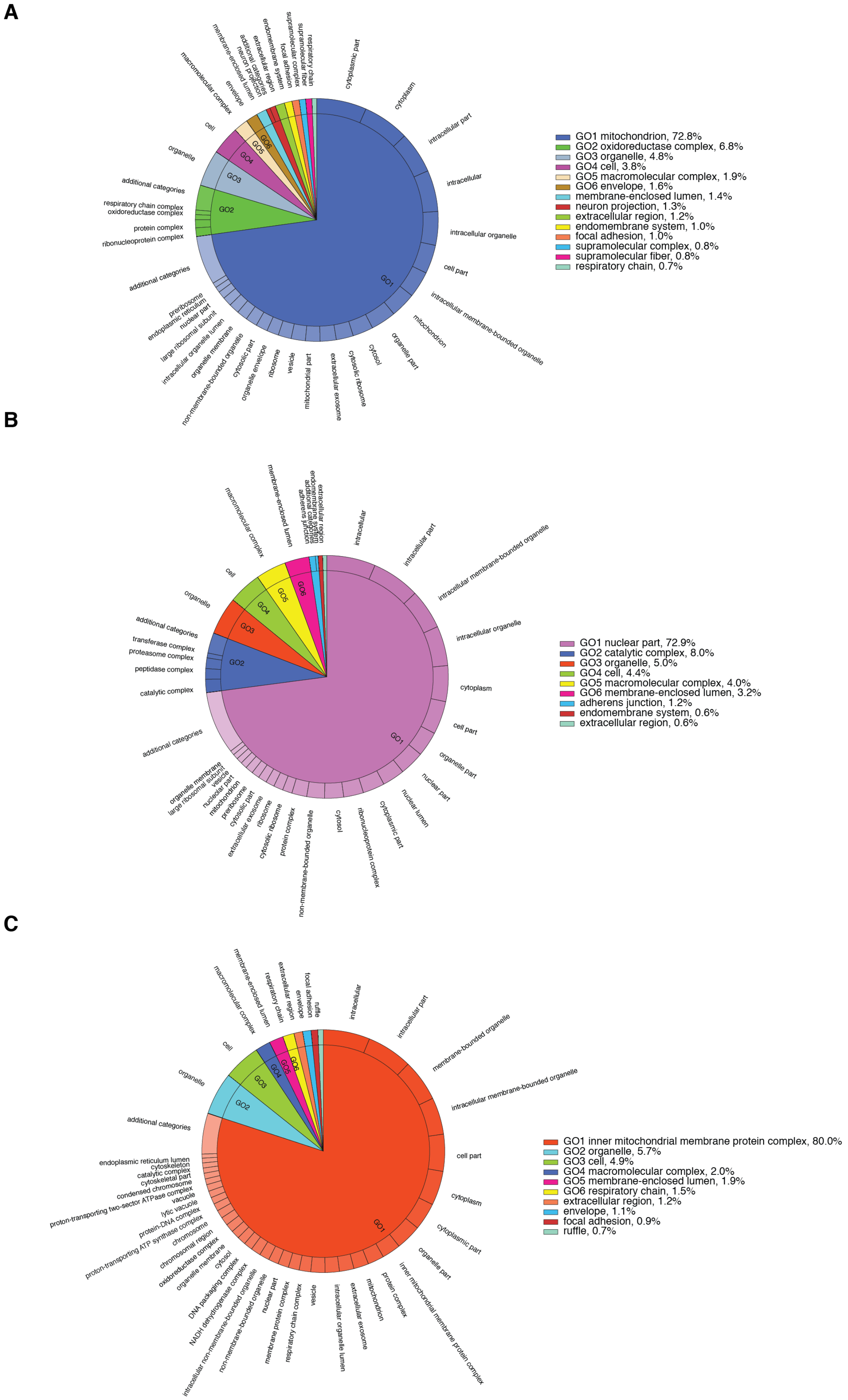
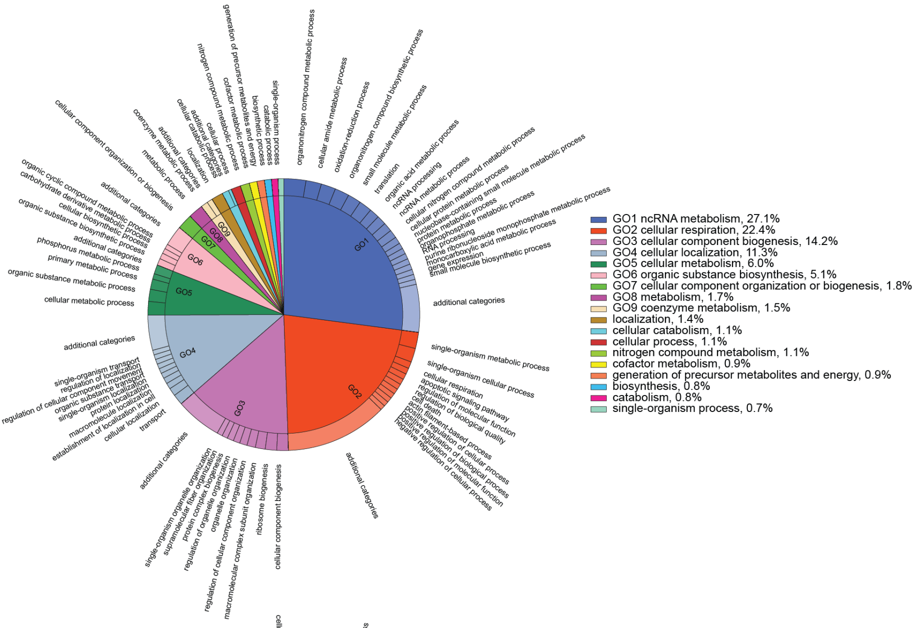

A
GO1 mitochondrion, 72.8%
GO2 oxidoreductase complex, 6.8%
GO3 organelle, 4.8%
GO4 cell, 3.8%
GO5 macromolecular complex, 1.9%
GO6 envelope, 1.6%
membrane-enclosed lumen, 1.4%
neuron projection, 1.3%
extracellular region, 1.2%
endomembrane system, 1.0%
focal adhesion, 1.0%
supramolecular complex, 0.8%
supramolecular fiber, 0.8%
respiratory chain, 0.7%
GO1
GO2
GO3
GO4
GO5
GO6
cytoplasmic part
cytoplasm
intracellular part
intracellular
intracellular organelle
cell part
intracellular membrane-bounded organelle
mitochondrion
organelle part
cytosol
cytosolic ribosome
extracellular exosome
mitochondrial part
vesicle
ribosome
organelle envelope
cytosolic part
non-membrane-bounded organelle
organelle membrane
intracellular organelle lumen
large ribosomal subunit
nuclear part
endoplasmic reticulum
preribosome
additional categories
ribonucleoprotein complex
protein complex
oxidoreductase complex
respiratory chain complex
additional categories
organelle
cell
macromolecular complex
envelope
membrane-enclosed lumen
neuron projection
additional categories
extracellular region
endomembrane system
focal adhesion
supramolecular complex
supramolecular fiber
respiratory chain
B
GO1 nuclear part, 72.9%
GO2 catalytic complex, 8.0%
GO3 organelle, 5.0%
GO4 cell, 4.4%
GO5 macromolecular complex, 4.0%
GO6 membrane-enclosed lumen, 3.2%
adherens junction, 1.2%
endomembrane system, 0.6%
extracellular region, 0.6%
GO1
GO2
GO3
GO4
GO5
GO6
intracellular
intracellular part
intracellular membrane-bounded organelle
intracellular organelle
cytoplasm
cell part
organelle part
nuclear part
nuclear lumen
cytoplasmic part
ribonucleoprotein complex
cytosol
non-membrane-bounded organelle
protein complex
cytosolic ribosome
ribosome
extracellular exosome
cytosolic part
preribosome
mitochondrion
nucleolar part
vesicle
large ribosomal subunit
organelle membrane
additional categories
catalytic complex
peptidase complex
proteasome complex
transferase complex
additional categories
organelle
cell
macromolecular complex
membrane-enclosed lumen
adherens junction
additional categories
endomembrane system
extracellular region
C
GO1 inner mitochondrial membrane protein complex, 80.0%
GO2 organelle, 5.7%
GO3 cell, 4.9%
GO4 macromolecular complex, 2.0%
GO5 membrane-enclosed lumen, 1.9%
GO6 respiratory chain, 1.5%
extracellular region, 1.2%
envelope, 1.1%
focal adhesion, 0.9%
ruffle, 0.7%
GO1
GO2
GO3
GO4
GO5
GO6
intracellular
intracellular part
membrane-bounded organelle
intracellular membrane-bounded organelle
cell part
cytoplasm
cytoplasmic part
organelle part
inner mitochondrial membrane protein complex
protein complex
mitochondrion
extracellular exosome
intracellular organelle lumen
vesicle
respiratory chain complex
membrane protein complex
nuclear part
non-membrane-bounded organelle
intracellular non-membrane-bounded organelle
NADH dehydrogenase complex
DNA packaging complex
cytosol
organelle membrane
oxidoreductase complex
chromosomal region
chromosome
proton-transporting ATP synthase complex
protein-DNA complex
lytic vacuole
vacuole
proton-transporting two-sector ATPase complex
condensed chromosome
cytoskeletal part
catalytic complex
cytoskeleton
endoplasmic reticulum lumen
additional categories
organelle
cell
macromolecular complex
membrane-enclosed lumen
respiratory chain
extracellular region
envelope
focal adhesion
ruffle

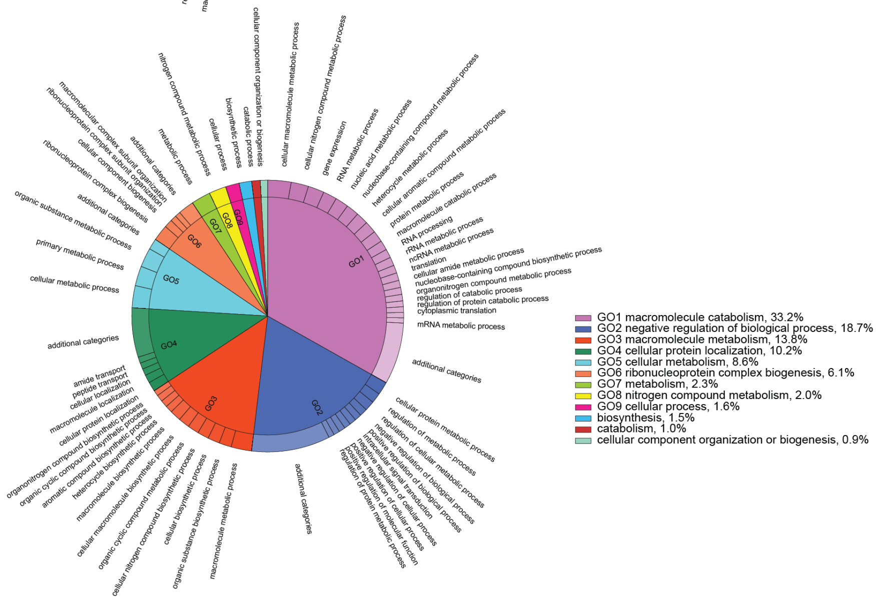
Figure S1. Related to Figures 3 and 5 | Loss of ELAC2 causes transcriptional changes in genes associated with both nuclear and mitochondrial function. Differential analyses were carried out on the RNA-Seq datasets and the significant changes in gene expression were identified and represented by gene ontologies. We used a two-layer hierarchy gene ontology circular visualization, where the inner circle represents the most affected GO categories. The outer circle is composed of one or more of the gene ontologies that are subcategories of the main GO category. Each category of the inner circle is shown in the legend and supported with the related colour and text identifier "GO" of the main category related to the outer ring. Each subcategory (outer ring) within the main category (inner ring) was sorted based on absolute $\log_{10}$ p-value from the smallest to largest, and a colour gradient is applied to highlight the largest to smallest value distribution to signify the greatest change found in the cellular component or process.

Gene ontologies are summarized for all the cellular compartment processes that are commonly altered between the *Elac2* and *Mrpp3* knockout mice compared to their respective controls (A), unique changes identified in the *Elac2* knockout mice compared to control mice (B) and unique changes identified in the *Mrpp3* knockout mice compared to control mice (C).

A


GO1 ncRNA metabolism, 27.1%
GO2 cellular respiration, 22.4%
GO3 cellular component biogenesis, 14.2%
GO4 cellular localization, 11.3%
GO5 cellular metabolism, 6.0%
GO6 organic substance biosynthesis, 5.1%
GO7 cellular component organization or biogenesis, 1.8%
GO8 metabolism, 1.7%
GO9 coenzyme metabolism, 1.5%
localization, 1.4%
cellular catabolism, 1.1%
cellular process, 1.1%
nitrogen compound metabolism, 1.1%
cofactor metabolism, 0.9%
generation of precursor metabolites and energy, 0.9%
biosynthesis, 0.8%
catabolism, 0.8%
single-organism process, 0.7%

B


GO1 macromolecule catabolism, 33.2%
GO2 negative regulation of biological process, 18.7%
GO3 macromolecule metabolism, 13.8%
GO4 cellular protein localization, 10.2%
GO5 cellular metabolism, 8.6%
GO6 ribonucleoprotein complex biogenesis, 6.1%
GO7 metabolism, 2.3%
GO8 nitrogen compound metabolism, 2.0%
GO9 cellular process, 1.6%
biosynthesis, 1.5%
catabolism, 1.0%
cellular component organization or biogenesis, 0.9%

C

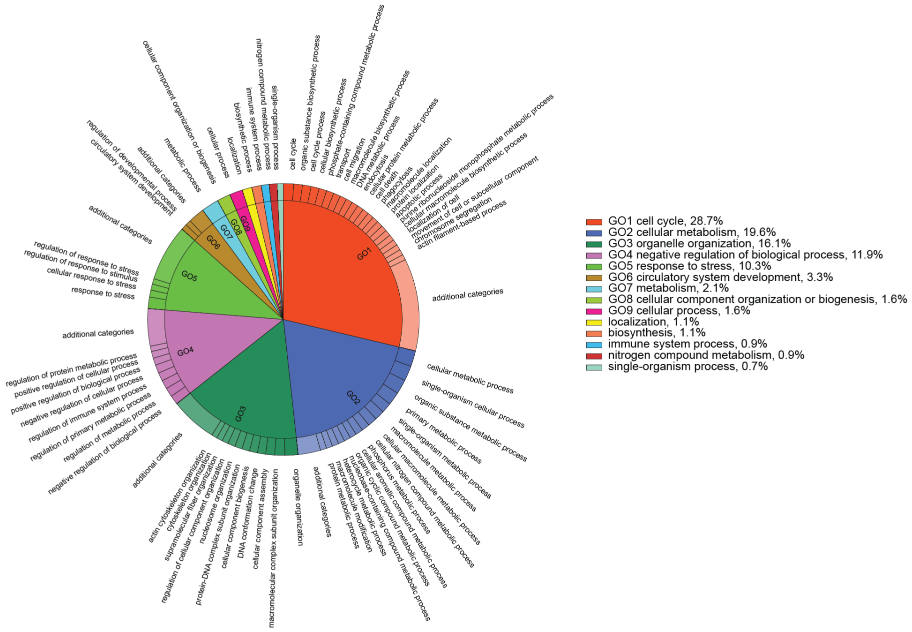
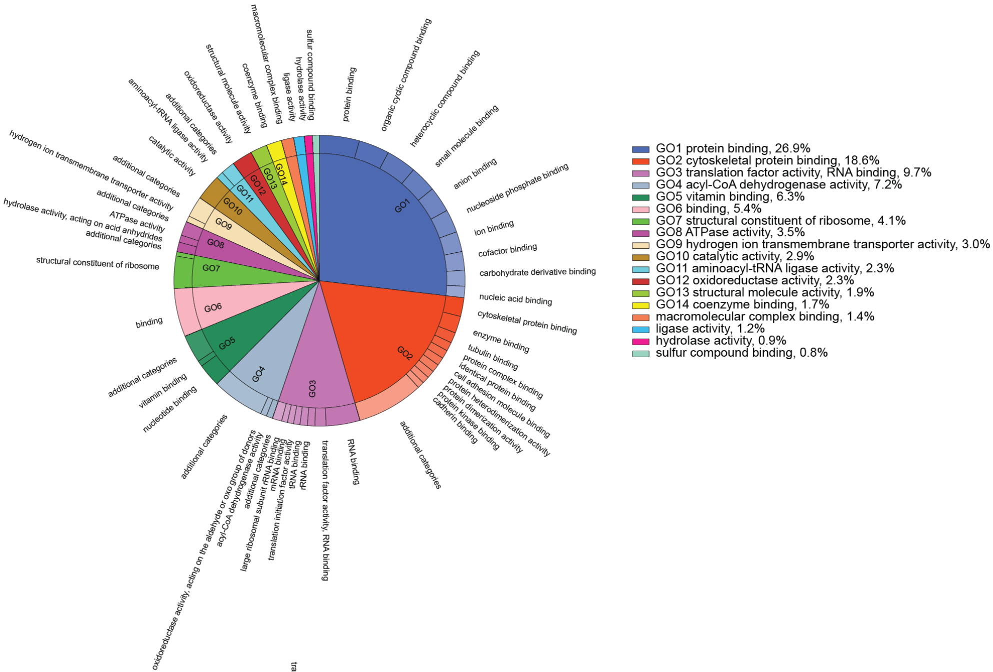
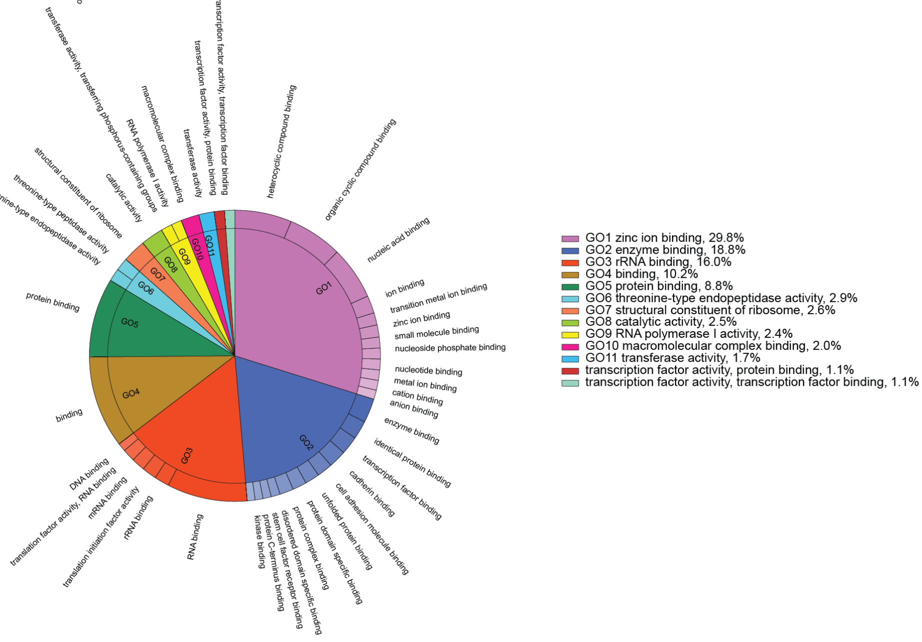

GO1 cell cycle, 28.7%
GO2 cellular metabolism, 19.6%
GO3 organelle organization, 16.1%
GO4 negative regulation of biological process, 11.9%
GO5 response to stress, 10.3%
GO6 circulatory system development, 3.3%
GO7 metabolism, 2.1%
GO8 cellular component organization or biogenesis, 1.6%
GO9 cellular process, 1.6%
localization, 1.1%
biosynthesis, 1.1%
immune system process, 0.9%
nitrogen compound metabolism, 0.9%
single-organism process, 0.7%

Figure S2. Related to Figures 3 and 5 | Loss of ELAC2 causes transcriptional changes in genes associated with both nuclear and mitochondrial function. Gene ontology summary of all biological processes that are commonly altered between the *Elac2* and *Mrpp3* knockout mice compared to their respective controls (A), unique changes identified in the *Elac2* knockout mice compared to control mice (B) and unique changes identified in the *Mrpp3* knockout mice compared to control mice (C).

A


GO1 protein binding, 26.9%
GO2 cytoskeletal protein binding, 18.6%
GO3 translation factor activity, RNA binding, 9.7%
GO4 acyl-CoA dehydrogenase activity, 7.2%
GO5 vitamin binding, 6.3%
GO6 binding, 5.4%
GO7 structural constituent of ribosome, 4.1%
GO8 ATPase activity, 3.5%
GO9 hydrogen ion transmembrane transporter activity, 3.0%
GO10 catalytic activity, 2.9%
GO11 aminoacyl-tRNA ligase activity, 2.3%
GO12 oxidoreductase activity, 2.3%
GO13 structural molecule activity, 1.9%
GO14 coenzyme binding, 1.7%
macromolecular complex binding, 1.4%
ligase activity, 1.2%
hydrolase activity, 0.9%
sulfur compound binding, 0.8%
protein binding
organic cyclic compound binding
heterocyclic compound binding
small molecule binding
anion binding
nucleoside phosphate binding
ion binding
cofactor binding
carbohydrate derivative binding
nucleic acid binding
cytoskeletal protein binding
enzyme binding
tubulin binding
protein complex binding
identical protein binding
cell adhesion molecule binding
protein heterodimerization activity
protein dimerization activity
protein kinase binding
cadherin binding
additional categories
RNA binding
translation factor activity, RNA binding
rRNA binding
tRNA binding
mRNA binding
translation initiation factor activity
large ribosomal subunit rRNA binding
additional categories
acyl-CoA dehydrogenase activity
oxidoreductase activity, acting on the aldehyde or oxo group of donors
additional categories
nucleotide binding
vitamin binding
additional categories
binding
structural constituent of ribosome
additional categories
hydrolase activity, acting on acid anhydrides
ATPase activity
additional categories
hydrogen ion transmembrane transporter activity
additional categories
catalytic activity
aminoacyl-tRNA ligase activity
additional categories
oxidoreductase activity
structural molecule activity
coenzyme binding
macromolecular complex binding
ligase activity
hydrolase activity
sulfur compound binding
GO1
GO2
GO3
GO4
GO5
GO6
GO7
GO8
GO9
GO10
GO11
GO12
GO13
GO14

B


GO1 zinc ion binding, 29.8%
GO2 enzyme binding, 18.8%
GO3 rRNA binding, 16.0%
GO4 binding, 10.2%
GO5 protein binding, 8.8%
GO6 threonine-type endopeptidase activity, 2.9%
GO7 structural constituent of ribosome, 2.6%
GO8 catalytic activity, 2.5%
GO9 RNA polymerase I activity, 2.4%
GO10 macromolecular complex binding, 2.0%
GO11 transferase activity, 1.7%
transcription factor activity, protein binding, 1.1%
transcription factor activity, transcription factor binding, 1.1%
heterocyclic compound binding
organic cyclic compound binding
nucleic acid binding
ion binding
transition metal ion binding
zinc ion binding
small molecule binding
nucleoside phosphate binding
nucleotide binding
metal ion binding
cation binding
anion binding
enzyme binding
identical protein binding
transcription factor binding
cadherin binding
cell adhesion molecule binding
unfolded protein binding
protein domain specific binding
protein complex binding
disordered domain specific binding
stem cell factor receptor binding
protein C-terminus binding
kinase binding
RNA binding
rRNA binding
translation initiation factor activity
mRNA binding
translation factor activity, RNA binding
DNA binding
binding
protein binding
threonine-type endopeptidase activity
threonine-type peptidase activity
structural constituent of ribosome
catalytic activity
transferase activity, transferring phosphorus-containing groups
RNA polymerase I activity
macromolecular complex binding
transferase activity
transcription factor activity, protein binding
transcription factor activity, transcription factor binding
GO1
GO2
GO3
GO4
GO5
GO6
GO7
GO8
GO9
GO10
GO11

C

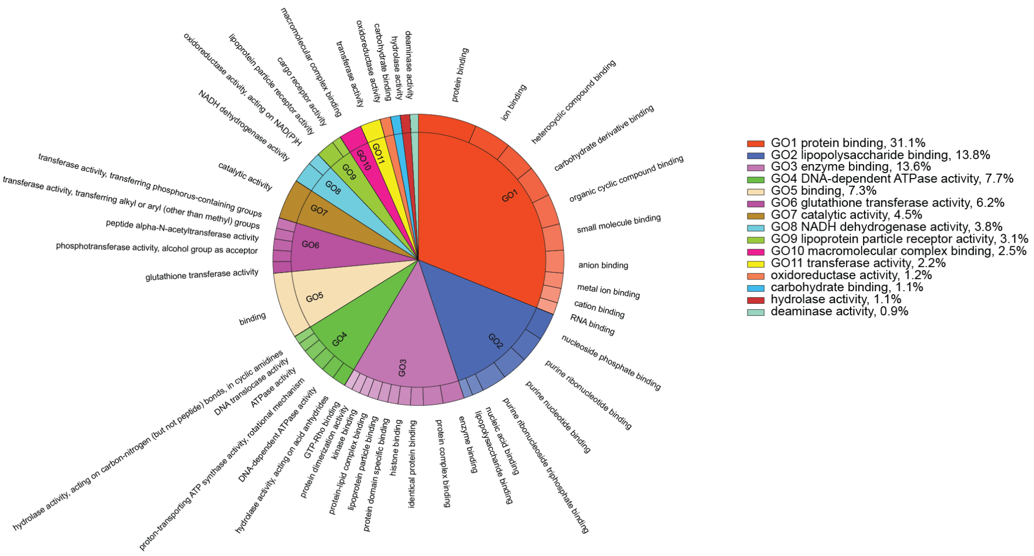

GO1 protein binding, 31.1%
GO2 lipopolysaccharide binding, 13.8%
GO3 enzyme binding, 13.6%
GO4 DNA-dependent ATPase activity, 7.7%
GO5 binding, 7.3%
GO6 glutathione transferase activity, 6.2%
GO7 catalytic activity, 4.5%
GO8 NADH dehydrogenase activity, 3.8%
GO9 lipoprotein particle receptor activity, 3.1%
GO10 macromolecular complex binding, 2.5%
GO11 transferase activity, 2.2%
oxidoreductase activity, 1.2%
carbohydrate binding, 1.1%
hydrolase activity, 1.1%
deaminase activity, 0.9%
protein binding
ion binding
heterocyclic compound binding
carbohydrate derivative binding
organic cyclic compound binding
small molecule binding
anion binding
metal ion binding
cation binding
RNA binding
nucleoside phosphate binding
purine ribonucleotide binding
purine nucleotide binding
purine ribonucleoside triphosphate binding
nucleic acid binding
lipopolysaccharide binding
enzyme binding
protein complex binding
identical protein binding
histone binding
protein domain specific binding
lipoprotein particle binding
protein-lipid complex binding
protein dimerization activity
kinase binding
GTP-Rho binding
hydrolase activity, acting on acid anhydrides
DNA-dependent ATPase activity
proton-transporting ATP synthase activity, rotational mechanism
ATPase activity
DNA translocase activity
hydrolase activity, acting on carbon-nitrogen (but not peptide) bonds, in cyclic amidines
binding
glutathione transferase activity
phosphotransferase activity, alcohol group as acceptor
peptide alpha-N-acetyltransferase activity
transferase activity, transferring alkyl or aryl (other than methyl) groups
transferase activity, transferring phosphorus-containing groups
catalytic activity
NADH dehydrogenase activity
oxidoreductase activity, acting on NAD(P)H
lipoprotein particle receptor activity
cargo receptor activity
macromolecular complex binding
transferase activity
oxidoreductase activity
carbohydrate binding
hydrolase activity
deaminase activity
GO1
GO2
GO3
GO4
GO5
GO6
GO7
GO8
GO9
GO10
GO11

Figure S3. Related to Figures 3 and 5 | Loss of ELAC2 causes transcriptional changes in genes associated with both nuclear and mitochondrial function. Gene ontology summary of all molecular functions that are commonly altered between the *Elac2* and *Mrpp3* knockout mice compared to their respective controls (A), unique changes identified in the *Elac2* knockout mice compared to control mice (B) and unique changes identified in the *Mrpp3* knockout mice compared to control mice (C).