Fig. S1. Oxidative modifications of cysteine

(A) The initial reaction of cysteine (C) with oxidants yields sulfenic acid (SOH). SOH can be further oxidized to generate sulfinic (SO₂H) and sulfonic (SO₃H) acid. (B) Serine (S) is similar to cysteine but cannot be oxidized, whereas aspartic acid (D) mimics sulfinic acid, a partially oxidized form of cysteine.
Fig. S2. Volcano Plots of RNAseq data

Log2fold changes in gene expression are plotted against -Log10(P value) where the P values are adjusted for multiple comparisons (Padj) using the method of (83). Points in black are significantly different between the conditions indicated in the graph titles (at a confidence level of Padj <0.05). Points in grey are not significantly different. In panels (B), (C) and (G), the grey points are not visible because of the data range plotted. Axes have been chosen to best represent the data. The number of genes that are significantly down-regulated and up-regulated are given in red and blue, respectively.
| Pathway | Genes upregulated in WT vs WT+HPQ (includes 19% of upregulated genes) | Genes downregulated in WT vs WT+HPQ (includes 3.8% of downregulated genes) |
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Fig. S3. PQ upregulates genes involved in development and growth and down-regulates genes involved in degradation, metabolic pathways, and energy generation

This Table shows all the KEGG pathways of genes significantly up- and down- regulated by PQ, obtained using the online analysis tool DAVID (Database for Annotation, Visualization, and Integrated Discovery; Version 6.8) (62, 63). 19% of up-regulated and 9.5% of down-regulated genes fall into defined KEGG pathways. When these KEGG pathways are placed into broad categories of biological processes it can be seen that PQ up-regulates development, growth, and quality control, while down-regulating processes involved in degradation and metabolism. KEGG pathways are biochemical pathways defined by the Kyoto Encyclopedia of Genes and Genomes (64). Counts represent the number of genes in the KEGG pathway that were among the list of significantly up or down-regulated genes. P-values are based on Fisher’s exact test to measure the gene-enrichment in the pathway. Padj represents adjusted p-values which control for false discovery rate with multiple comparisons using the method of (83). A shortened and simplified depiction of this analysis is presented in Fig. 2.
Fig. S4. The Spliceosome KEGG pathway
Proteins with homologs in C. elegans are shaded in green. Proteins which are encoded by genes that are significantly up-regulated by PQ treatment are indicated with a red star. Genes encoding 101/106 proteins in the pathway are up-regulated by PQ treatment. KEGG pathway cel03040 reproduced with permission (64).
Fig. S5. The Citrate Cycle (TCA cycle) KEGG pathway
Enzymes with homologs in C. elegans are shaded in green. Enzymes which are encoded by genes that are significantly down-regulated by PQ treatment are indicated with a red star. Genes encoding 18/33 enzymes in the pathway are down-regulated by PQ treatment. KEGG pathway cel00020 reproduced with permission (64).
Fig. S6. The Proteasome KEGG pathway
Subunits with homologs in *C. elegans* are shaded in green. Subunits which are encoded by genes that are significantly up-regulated by PQ treatment are indicated with a red star. Genes encoding 35/38 subunits with homologues in *C. elegans* are up-regulated by PQ treatment. KEGG pathway cel03050 reproduced with permission (64).
Fig. S7. Ribosome Biogenesis in Eukaryotes KEGG Pathway
Proteins with homologs in *C. elegans* are shaded in green. Proteins which are encoded by genes that are significantly up-regulated by PQ treatment are indicated with a red star. Genes encoding 49/78 proteins with subunits in *C. elegans* are up-regulated by PQ treatment. KEGG pathway cel03008 reproduced with permission (64).
Fig. S8. Mismatch Repair KEGG Pathway
Proteins with homologs in *C. elegans* are shaded in green. Proteins which are encoded by genes that are significantly up-regulated by PQ treatment are indicated with a red star. Genes encoding 16/18 proteins with homologues in *C. elegans* are up-regulated by PQ treatment. KEGG pathway cel03430 reproduced with permission (64).
Fig. S9. Glycolysis/Gluconeogenesis KEGG pathway

Enzymes with homologs in *C. elegans* are shaded in green. Enzymes which are encoded by genes that are significantly down-regulated by PQ treatment are indicated with a red star. Genes encoding 16/39 enzymes with homologues in *C. elegans* are down-regulated by PQ treatment. KEGG pathway cel00010 reproduced with permission (64).
Fig. S10. Peroxisome KEGG pathway
Proteins with homologs in *C. elegans* are shaded in green. Proteins which are encoded by genes that are significantly down-regulated by PQ treatment are indicated with a red star. Genes encoding 30/63 proteins with homologues in *C. elegans* are down-regulated by PQ treatment. KEGG pathway cel04146 reproduced with permission (64).
Fig. S11. Valine, Leucine, and Isoleucine Degradation KEGG pathway

Enzymes with homologs in *C. elegans* are shaded in green. Enzymes which are encoded by genes that are significantly down-regulated by PQ treatment are indicated with a red star. Genes encoding 33/40 enzymes with homologues in *C. elegans* are down-regulated by PQ treatment. KEGG pathway cel00280 reproduced with permission (64).
**Fig. S12.** PQ does not require the AMPK or TOR signaling pathways to increase lifespan but may involve these pathways to affect protein and ATP levels.

(A) Lifespan of *aak-2(ok524)* mutants treated with 0.1 mM PQ from hatching. (B) Lifespan of *raga-1(ok386)* mutants treated with 0.1 mM PQ from hatching. (C) Lifespan of *rsks-1(ok524)* mutants treated with 0.1 mM PQ from hatching. (D) Protein levels normalized to the mean level of untreated WT (58.60 ± 4.20 µg). (E) ATP levels normalized to the mean level of untreated WT (15.91 ± 0.84 pmol/µg protein). For (A-C) numerical values and statistics are presented in Table S1. For (D, E) bars represent means and error bars SEM, and the individual points are also plotted. Phenotypes of untreated and treated mutants are compared to untreated and treated WT, respectively, and significant differences are indicated above the bars with # (## $p<0.01$, #### $p<0.0001$). For each genotype, the untreated and treated phenotypes were also compared, and significant differences are indicated above the set of bars with asterisks (**$p<0.01$, ***$p<0.001$, ****$p<0.0001$).
Fig. S13. Comparison of gene expression changes brought about by treatment of the WT with PQ and in long-lived mutants

One measure of how similar gene sets A and B are to each other is the percentage of genes that are common out of the total number of genes changed in either of the two sets (A U B). These percentages are what are shown in the table, which compares the genes sets changed by PQ treatment to the genes sets changed by various mutations as well as comparing the genes sets changed by the mutations to each other. When the percentage of genes changed is in the same direction (up or down) in the two sets being compared is 2- or more times greater than the percentage changed in the opposite direction the cell is shaded in pink. When the percentage of genes changed in the opposite direction in the two sets being compared is two or more times greater than the percentage changed in the same direction the cell is shaded in blue. The cells are shaded in yellow when the difference between the percentages corresponding to the two types of comparisons is not two-fold or greater. As shown in Fig. 6, when compared to the classical aging genes *daf-2*, *eat-2*, *glp-1*, *rsks-1* and *nuo-6*, PQ treatment tends to change many more genes in the opposite direction than in the same directions (blue cells rather than pink cells). In contrast, *pcca-1* and *metr-1* gene expression tends to be changed in the same direction (pink cells). There is no clear pattern for *isp-1*. As expected, comparison between *pcca-1* and *metr-1* and the aging genes partially reflects the similarity between their pattern of expression and that of PQ treatment: a preponderance of blue cells. However, when we only consider comparisons between gene expression changes among the long-lived mutants (in the box outlined in thick black lines), gene expression changes for genes in overlaps are almost entirely in the same direction, except for *isp-1* compared to *eat-2*, which shows no clear pattern.
Fig. S14. A model of how RDRS affects gene expression

This figure is an elaboration of the model shown in Fig. 7, depicting the situation in the WT, as well as in C118S and C118D mutants, in the absence and presence of PQ treatment. (A) The situation in the WT. LET-60ras signaling leads, directly or indirectly, to the production of ROS, hereafter referred to as RAS-dependent ROS signaling (RDRS), which affects gene expression. RDRS promotes the expression of genes associated with growth and the high-quality synthesis of cellular constituents (referred to as Growth and Quality) and inhibits the expression of genes necessary for intermediary metabolism and energy generation (referred to as Metabolism). Signaling through the RAS pathway is negatively regulated by oxidation of cysteine C118 of LET-60ras. This effect, which requires SOD-1, appears to act as negative feedback from RDRS (red arrow). (B) The situation in C118S mutants. C118S cannot be oxidized by ROS. In the absence of negative feedback from RDRS, RAS signaling is increased, leading to an increase in RDRS and thus, to an up-regulation of genes associated with Growth and Quality, and a down-regulation of genes necessary for Metabolism. (C) The situation in C118D mutants. C118D mimics C118 oxidation and is likely resistant or insensitive to feedback regulation. However, as it mimics oxidized C118 it leads to a downregulation of RAS signaling and a decrease of RDRS. This reveals the existence of an opposing signaling pathway (X) that affects global gene expression but acts in the opposite direction from RAS. In the absence of strong RDRS, the unknown X pathway dominates, which results in a down-regulation of genes associated with Growth and Quality, and an up-regulation of genes necessary for Metabolism. (D) The situation in the WT treated with PQ. ROS generated by PQ acts downstream of LET-60ras to enhance RDRS resulting in an up-regulation of genes associated with Growth and Quality, and a down-regulation of genes necessary for Metabolism. RDRS is increased to a higher degree than in C118S mutants, despite a possible increase in the negative feedback through C118. As described, PQ in a SOD-1-dependant manner, is also capable of oxidizing C118. However, this does not affect the stimulation of RDRS by PQ, given that it acts downstream of LET-60ras. (E) The situation in C118S mutants treated with PQ. The absence of the normal feedback provided by oxidation of C118 leads to chronic activation of LET-60ras. This activates a signal-dampening mechanism, which are well-known to exist downstream of RAS signaling. We expect this mechanism to be a normal part of RDRS, but its importance is most obviously revealed in C118S mutants treated with PQ, which is why it is only shown for this situation. When C118S mutants are treated with PQ, the dampening mechanism prevents the
artificial elevation of ROS by PQ to have major effects on gene expression in C118S mutants. The dampening of the effect of PQ in the mutants appears to be more pronounced for up-regulated genes than for down-regulated genes. (F) The situation in C118D mutants treated with PQ. As discussed above, RAS signaling is down-regulated in C118D mutants, but because it acts downstream of LET-60, PQ can nonetheless enhance RDRS. Thus, the weakened LET-60 ras signal is bypassed with an intense downstream ROS signal, which overcomes the effect of X and produces a pattern of gene expression similar to that of the WT treated with PQ.
**Table S1.** Numerical values and statistics for aging data presented in Fig. 1 and Fig. S12.

| Genotype                      | Sample size N (repeats) | Mean Lifespan ± SEM | P value (significance) a,b |
|-------------------------------|-------------------------|---------------------|---------------------------|
| WT                            | 150 (3)                 | 20.45 ± 0.31        |                           |
| sod-1(tm783)                  | 150 (3)                 | 17.87 ± 0.34        | WT: 0.0001 (****)         |
| sod-2(ok1030)                 | 150 (3)                 | 28.43 ± 0.47        | WT: 0.0001 (****)         |
| sod-1; sod-2                  | 100 (2)                 | 17.82 ± 0.40        | sod-1(tm783): 0.999 (ns)  |
|                               |                         |                     | sod-2(ok1030): 0.0001 (****) |
| WT                            | 150 (3)                 | 20.45 ± 0.31        |                           |
| sod-1(tm783)                  | 150 (3)                 | 17.87 ± 0.34        | WT: 0.0001 (****)         |
| ctl-1(ok1242)                 | 150 (3)                 | 19.81 ± 0.37        | WT: 0.8597 (ns)           |
| ctl-2(ok1137)                 | 150 (3)                 | 19.64 ± 0.35        | WT: 0.5986 (ns)           |
| ctl-3(ok2042)                 | 150 (3)                 | 20.08 ± 0.35        | WT: 0.9965 (ns)           |
| sod-1 ctl-1                   | 100 (2)                 | 20.06 ± 0.46        | sod-1(tm783): 0.0001 (****) |
| sod-1 ctl-2                   | 100 (2)                 | 19.34 ± 0.37        | WT: 0.30947 (ns)          |
| sod-1 ctl-3                   | 100 (2)                 | 18.54 ± 0.33        | sod-1(tm783): 0.0130 (*)  |
|                               |                         |                     | sod-1(tm783): 0.4382 (ns) |
| WT                            | 150 (3)                 | 20.45 ± 0.31        |                           |
| WT + 0.1mM PQ                 | 150 (3)                 | 25.01 ± 0.44        | WT: 0.0001 (****)         |
| sod-1(tm783)                  | 150 (3)                 | 17.87 ± 0.34        | sod-1: 0.07 (ns)          |
| sod-1(tm783) + 0.1mM PQ       | 150 (3)                 | 19.17 ± 0.36        | sod-1: 0.07 (ns)          |
| sod-1(tm783)                  | 150 (3)                 | 17.32 ± 0.22        | sod-1: 0.07 (ns)          |
| sod-1(tm783) + 0.1mM PQ       | 100 (2)                 | 22.54 ± 0.47        | sod-3: 0.0001 (****)      |
| sod-4(gk101)                  | 150 (3)                 | 19.29 ± 0.33        | sod-4: 0.0001 (****)      |
| sod-4(gk101) + 0.1mM PQ       | 150 (3)                 | 24.43 ± 0.44        | sod-4: 0.0001 (****)      |
| sod-5(tm1146)                 | 150 (3)                 | 19.73 ± 0.32        | sod-5: 0.0001 (****)      |
| sod-5(tm1146) + 0.1mM PQ      | 150 (3)                 | 25.23 ± 0.47        | sod-5: 0.0001 (****)      |
| WT                            | 100 (2)                 | 19.14 ± 0.33        |                           |
| WT + 0.1mM PQ                 | 100 (2)                 | 26.74 ± 0.56        | WT: 0.0001 (****)         |
| let-60–C118S                  | 100 (2)                 | 18.86 ± 0.29        | WT: 0.9778 (ns)           |
| Strain | n (treatment) | Mean ± SD | p-value |
|--------|---------------|-----------|---------|
| let-60–C118S + 0.1mM PQ | 100 (2) | 22.16 ± 0.32 | WT + 0.1mM PQ: 0.0001(****) let-60–C118S: 0.0001(****) |
| WT | 100 (2) | 17.87 ± 0.26 | |
| WT + 0.1mM PQ | 100 (2) | 25.66 ± 0.39 | WT: 0.0001(****) |
| let-60–C118D | 100 (2) | 19.06 ± 0.32 | WT: 0.0512(ns) |
| let-60–C118D + 0.1mM PQ | 100 (2) | 25.57 ± 0.42 | WT + 0.1mM PQ: 0.9996 (ns) let-60–C118D: 0.0001(****) |

| Strain | n (treatment) | Mean ± SD | p-value |
|--------|---------------|-----------|---------|
| WT | 200 (4) | 19.18 ± 0.14 | |
| nuo-6(qm200) | 200 (4) | 37.89 ± 0.45 | WT: 0.0001(****) |
| let-60–C118S | 200 (4) | 18.92 ± 0.14 | WT: 0.19(ns) |
| nuo-6; let-60–C118S | 200 (4) | 21.42 ± 0.21 | WT: 0.0001(****) nuo-6: 0.0001(****) |

| Strain | n (treatment) | Mean ± SD | p-value |
|--------|---------------|-----------|---------|
| WT | 100 (2) | 21.54 ± 0.26 | |
| WT + 0.1mM PQ | 100 (2) | 24.60 ± 0.35 | WT: 0.0001(****) |
| aak-2(ok524) | 100 (2) | 18.74 ± 0.20 | WT: 0.0001(****) |
| aak-2(ok524) + 0.1mM PQ | 100 (2) | 20.86 ± 0.25 | aak-2: 0.0001(****) |

| Strain | n (treatment) | Mean ± SD | p-value |
|--------|---------------|-----------|---------|
| WT | 100 (2) | 21.24 ± 0.26 | |
| WT + 0.1mM PQ | 100 (2) | 23.80 ± 0.29 | WT: 0.0001(****) |
| raga-1(ok386) | 100 (2) | 28.00 ± 0.45 | WT: 0.0001(****) |
| raga-1(ok386) + 0.1mM PQ | 100 (2) | 33.71 ± 0.53 | raga-1: 0.0001(****) |

| Strain | n (treatment) | Mean ± SD | p-value |
|--------|---------------|-----------|---------|
| WT | 100 (2) | 21.54 ± 0.26 | |
| WT + 0.1mM PQ | 100 (2) | 24.60 ± 0.35 | WT: 0.0001(****) |
| rsks-1(ok1255) | 100 (2) | 25.99 ± 0.42 | WT: 0.0001(****) |
| rsks-1(ok1255) + 0.1mM PQ | 100 (2) | 35.20 ± 0.69 | rsks-1: 0.0001(****) |

aP-values are from One-way Anova. Significance thresholds are adjusted for multiple comparisons using the Šídák method.
bThe control to which the experimental strain/condition is compared is indicated.
| Cellular component (CC) Gene Ontology (GO) terms of genes Up-regulated by PQ | Count | P-Value | Benjamini |
|---|---|---|---|
| nucleus | 1014 | 1.3E-144 | 8.3E-142 |
| cytoplasm | 743 | 3.0E-75 | 1.2E-72 |
| nucleolus | 88 | 3.3E-30 | 2.4E-28 |
| cell cortex | 87 | 5.9E-23 | 3.9E-20 |
| chromosome | 78 | 2.1E-19 | 1.3E-20 |
| cytosol | 166 | 4.0E-21 | 5.0E-19 |
| nucleus | 46 | 1.0E-20 | 3.0E-19 |
| P granule | 54 | 3.2E-20 | 2.6E-18 |
| mitochondrion | 207 | 1.0E-19 | 8.1E-18 |
| proteasome complex | 35 | 3.0E-17 | 4.4E-15 |
| spliceosomal complex | 37 | 4.0E-16 | 2.6E-14 |
| condensed chromosome | 33 | 7.6E-16 | 4.1E-14 |
| catalytic step 2 spliceosome | 36 | 1.4E-14 | 6.4E-13 |
| kinesin motor complex | 21 | 1.3E-14 | 6.4E-13 |
| nuclear pore complex | 39 | 1.4E-12 | 5.0E-11 |
| nuclear envelope | 37 | 7.6E-09 | 3.0E-08 |
| chromatin, centromeric region | 24 | 4.1E-09 | 1.5E-08 |
| Golgi apparatus | 83 | 5.6E-12 | 1.9E-10 |
| condensed chromosome kinetochore | 33 | 1.4E-11 | 4.6E-10 |
| perinuclear region of cytoplasm | 50 | 2.7E-11 | 8.3E-10 |
| presecretory spliceosome | 23 | 1.1E-10 | 3.5E-09 |
| spindle | 26 | 1.3E-10 | 3.6E-09 |
| mitochondrial large ribosomal subunit | 21 | 1.6E-10 | 4.4E-09 |
| small subunit ribonucleoprotein | 28 | 2.5E-10 | 9.4E-09 |
| centrosome | 36 | 3.9E-10 | 9.7E-09 |
| endoplasmic reticulum | 119 | 9.2E-09 | 1.2E-08 |
| mitofusin organizing center | 22 | 2.4E-09 | 5.4E-08 |
| endoplasmic reticulum membrane | 77 | 2.4E-09 | 5.4E-08 |
| nuclear envelope | 33 | 3.1E-09 | 7.0E-08 |
| Golgi membrane | 58 | 1.1E-08 | 2.4E-07 |
| U4-U6-U5 tri-snRNP complex | 17 | 1.1E-08 | 4.2E-07 |
| mitochondrial small ribosomal subunit | 21 | 3.2E-08 | 2.4E-07 |
| DNA-directed RNA polymerase II complex | 16 | 7.1E-08 | 1.6E-07 |
| U2 snRNP | 17 | 1.4E-07 | 2.6E-06 |
| U1 snRNP | 16 | 4.2E-07 | 7.3E-06 |
| mediator complex | 17 | 6.4E-07 | 1.0E-05 |
| U2-type spliceosome | 14 | 7.7E-07 | 1.2E-05 |
| pre-mRNA splicing complex | 14 | 7.7E-07 | 1.2E-05 |
| DNA-directed RNA polymerase II core complex | 14 | 7.4E-07 | 1.2E-05 |
| nuclear exosome (RNase complex) | 13 | 2.9E-06 | 3.4E-05 |
| endosome | 26 | 3.9E-06 | 5.4E-05 |
| microtubule | 30 | 4.2E-06 | 6.4E-05 |
| cleavage furrow | 15 | 5.7E-06 | 5.4E-05 |
| perinuclear large subunit precursor | 20 | 6.9E-06 | 1.0E-04 |
| intracellular ribonuclease complex | 57 | 9.3E-06 | 1.0E-04 |
| spindle midzone | 15 | 1.3E-06 | 1.8E-04 |
| integral component of endoplasmic reticulum membrane | 21 | 1.4E-05 | 1.3E-04 |
| nuclear chromatin | 14 | 1.1E-05 | 2.0E-04 |
| spindle pole | 14 | 1.0E-05 | 2.0E-04 |
| collagen I | 76 | 1.0E-05 | 2.4E-04 |
| nuclear membrane | 16 | 2.0E-05 | 2.5E-04 |
| translation factor IF2/IF3 complex | 11 | 2.1E-05 | 3.6E-04 |
| mitotic spindle | 12 | 4.0E-05 | 4.6E-04 |
| pre-mRNA splicing particle, base subcomplex | 12 | 4.0E-05 | 4.6E-04 |
| U2 snRNP | 12 | 4.0E-05 | 4.6E-04 |
| ribosome | 89 | 4.8E-05 | 5.5E-04 |
| cytoplasmic exosome (RNase complex) | 10 | 8.5E-05 | 9.4E-04 |
| nuclear periphery | 10 | 8.7E-05 | 9.4E-04 |
| spindle microtubule | 10 | 8.7E-05 | 9.4E-04 |
| eukaryotic 40S preinitiation complex | 11 | 1.0E-04 | 1.3E-03 |
| cytosolic vesicle | 30 | 1.0E-04 | 1.8E-03 |
| g-hex nuclear | 9 | 2.8E-04 | 7.0E-03 |
| centrosome | 9 | 2.8E-04 | 7.0E-03 |
|核心 | 10 | 2.9E-04 | 7.0E-03 |
| DNA-directed RNA polymerase I complex | 10 | 3.8E-04 | 8.8E-03 |
| eukaryotic 48S preinitiation complex | 11 | 3.9E-04 | 8.8E-03 |
| P/B9 complex | 7 | 8.0E-04 | 5.0E-03 |
| U4 snRNP | 8 | 8.0E-04 | 5.0E-03 |
| core nucleator complex | 8 | 8.0E-04 | 5.0E-03 |
| COP9 signalosome | 8 | 8.0E-04 | 5.0E-03 |
| eukaryotic translation initiation factor 3 complex | 12 | 9.1E-04 | 8.3E-03 |
| signal complex | 9 | 1.0E-03 | 9.3E-03 |
| cytoplasmic acid vesicle membrane | 10 | 1.0E-03 | 9.3E-03 |
| nuclear chromatin, telomeric region | 10 | 1.0E-03 | 9.3E-03 |
| ubiquitin ligase complex | 15 | 1.0E-03 | 1.4E-02 |
| endoplasmic membrane | 12 | 1.0E-03 | 1.4E-02 |
| SCF ubiquitin ligase complex | 10 | 8.0E-03 | 1.7E-02 |
| phagocytic vesicle | 10 | 8.0E-03 | 1.7E-02 |
| early endosome | 7 | 2.0E-03 | 2.0E-02 |
| cortical granule | 7 | 2.0E-03 | 2.0E-02 |
| vacuolar complex | 7 | 2.0E-03 | 2.0E-02 |
| pre-mRNA splicing particle complex, alpha-subunit complex | 7 | 2.0E-03 | 2.0E-02 |
| Golgi transport complex | 7 | 2.0E-03 | 2.0E-02 |
| actin filament plate | 7 | 2.0E-03 | 2.0E-02 |
| previation fork protection complex | 7 | 2.0E-03 | 2.0E-02 |
| spliceosomal U1-UCRFP complex | 7 | 2.0E-03 | 2.0E-02 |
| spliceosome (RNase complex) | 7 | 2.0E-03 | 2.0E-02 |
| pre-mRNA splicing particle, telomerase complex | 7 | 2.0E-03 | 2.0E-02 |
| late endosome membrane | 8 | 3.0E-03 | 2.1E-02 |
| mitochondrial ribosome | 8 | 3.0E-03 | 2.1E-02 |
| nuclear proteasome complex | 8 | 3.0E-03 | 2.1E-02 |
| intracellular | 138 | 4.2E-03 | 5.9E-02 |
Table S2 shows the GO CC terms of genes significantly up-regulated by PQ, obtained using the online analysis tool DAVID (Database for Annotation, Visualization, and Integrated Discovery; version 6.8) (62, 63). 3222 (59.0%) of the up-regulated genes are represented by these terms. However, in the Table only GO CC terms with a Padj < 0.05 are shown. P-values are based on Fisher’s exact test to measure the gene-enrichment in the pathway. Padj represents adjusted p-values which control for false discovery rate with multiple comparisons by using the linear step-up method of (83).
Table S3. Gene Ontology Cellular Component Terms (GO_CC) for genes down-regulated by PQ

| Cellular component (CC) Gene Ontology (GO) terms of genes Down-regulated by PQ | Count | P-Value  | Benjamini |
|-----------------------------------------------------------------------------|-------|----------|-----------|
| extracellular space                                                         | 142   | 7.00E-26 | 2.20E-23  |
| pseudopodium                                                               | 36    | 9.70E-18 | 1.50E-15  |
| extrinsic component of cytoplasmic side of plasma membrane                 | 32    | 1.60E-10 | 1.70E-08  |
| intracellular membrane-bounded organelle                                    | 60    | 7.10E-10 | 5.50E-08  |
| cytoskeleton                                                                | 98    | 9.20E-10 | 5.70E-08  |
| membrane raft                                                               | 42    | 3.80E-09 | 2.00E-07  |
| extracellular region                                                        | 129   | 4.80E-09 | 2.10E-07  |
| peroxisome                                                                  | 25    | 4.80E-07 | 1.90E-05  |
| basement membrane                                                           | 15    | 8.80E-06 | 2.90E-04  |
| M band                                                                      | 19    | 9.30E-06 | 2.90E-04  |
| striated muscle dense body                                                  | 43    | 1.40E-05 | 4.00E-04  |
| lysosome                                                                    | 33    | 3.00E-04 | 7.80E-03  |
| myofibril                                                                   | 10    | 3.30E-04 | 7.80E-03  |
| chloride channel complex                                                    | 18    | 4.60E-04 | 1.00E-02  |
| proteinaceous extracellular matrix                                          | 17    | 1.60E-03 | 3.20E-02  |

**Table S3** shows all the GO CC terms of genes significantly down-regulated by PQ, obtained using the online analysis tool DAVID (Database for Annotation, Visualization, and Integrated Discovery; version 6.8) [(62, 63)](). 2788 (56.9%) of the down-regulated genes are represented by these terms, However, in the Table only GO CC terms with a Padj < 0.05 are shown. P-values are based on Fisher’s exact test to measure the gene-enrichment in the pathway. Padj represents adjusted p-values which control for false discovery rate with multiple comparisons by using the linear step-up method of [(83)].
Other Supplementary Materials for this manuscript includes the following file:

Data S1: Significantly Changed Genes.xlsx

This Excel file contains the names of the genes that were significantly up-regulated and down-regulated in the RNAseq analyses carried out in this study.