

Table S1. Model reactions and reaction rates.

| Reaction Name            | Description                                                             | Reaction                       | Parameter  | Type  | Value/range           | Unit        | Reference |
|--------------------------|-------------------------------------------------------------------------|--------------------------------|------------|-------|-----------------------|-------------|-----------|
| Transcription            | Transcription as a single step                                          | Gene -> mRNA                   | $k_T$      | free  | [1e-5, 1]             | 1/s         | (1)       |
| Translation_1            | Translation up to UGA codon                                             | mRNA -> mRNA.UGA               | $k_1$      | fixed | 25/(#codons to UGA)   | 1/s         | (2)       |
| tRNAsec Binding          | Binding of tRNAsec to mRNA                                              | mRNA.UGA + tRNAsec -> mRNA.sec | $k_2$      | free  | [1e-7,1]              | ml/(mmol*s) |           |
| Translation_2            | Translation from UGA codon to termination                               | mRNA.sec -> tRNAsec + mRNA     | $k_{sec}$  | fixed | 25/(#codons from UGA) | 1/s         | (2)       |
| NMD                      | Premature termination at UGA codon, followed by nonsense-mediated decay | mRNA.UGA ->                    | $k_{NMD}$  | free  | [1e-7,10]             | 1/s         | (1,3)     |
| Background Degradation 1 | Degradation of mRNA with ribosome at UGA                                | mRNA.UGA ->                    | $k_D$      | fixed | 2.5e-4                | 1/s         | (1)       |
| Background Degradation 2 | Degradation of free mRNA                                                | mRNA ->                        | $k_D$      | fixed | 2.5e-4                | 1/s         | (1)       |
| Background Degradation 3 | Degradation of mRNA with ribosome after UGA                             | mRNA.sec ->                    | $k_D$      | fixed | 2.5e-4                | 1/s         | (1)       |
| Ribosome drop-off        | Normal termination at premature UGA codon                               | mRNA.UGA->mRNA                 | $k_{DROP}$ | free  | [2.5e-4,1e2]          | 1/s         | (1,3)     |

## References

1. Schwanhaussner, B., Busse, D., Li, N., Dittmar, G., Schuchhardt, J., Wolf, J., Chen, W. and Selbach, M. (2011) Global quantification of mammalian gene expression control. *Nature*, **473**, 337-342.
2. Ingolia, N., Lareau, L. and Weissman, J. (2011) Ribosome profiling of mouse embryonic stem cells reveals the complexity and dynamics of mammalian proteomes. *Cell*, **147**, 789-802.
3. Trcek, T., Sato, H., Singer, R. and Maquat, L. (2013) Temporal and spatial characterization of nonsense-mediated mRNA decay. *Genes & development*, **27**, 541-551.

Table S2. Primers for rtPCR.

| Gene          | primer       | sequence                          | Annealing Temperature (°C) |
|---------------|--------------|-----------------------------------|----------------------------|
| <i>GPX1</i>   | hGPX1RT-Fwd  | 5'-CAAGAACGAAGAGATTCTGAATT-3'     | 60                         |
|               | hGPX1RT-Rev  | 5'-CACTTCTCGAAGAGCATGAA-3'        |                            |
| <i>GPX2</i>   | hGPx2RT-Fwd  | 5'-GACATCAGGAGAACTGTCAGAA-3'      | 60                         |
|               | hGPX2RT-Rev  | 5'-CATTTTTGGACAAGGGTGAAG-3'       |                            |
| <i>GPX4</i>   | hGPX4RT-Fwd  | 5'-CGATACGCTGAGTGTGGTTTGC-3'      | 60                         |
|               | hGPX4RT-Rev  | 5'-CATTTCCCAGGATGCCCTTG-3'        |                            |
| <i>SELH</i>   | hSelHRT-Fwd  | 5'-TTGTTATCGAGCATTGCACTAGC-3'     | 60                         |
|               | hSelHRT-Rev  | 5'-AACTCTTCCACCACCTCTTGAG-3'      |                            |
| <i>SELK</i>   | hSelKRT-Fwd  | 5'-TGGAAGAGGGCCACCAGGAA-3'        | 60                         |
|               | hSelKRT-Rev  | 5'-ATGCGCATGTCCGGTTGTCT-3'        |                            |
| <i>SEP15</i>  | hSeP15RT-Fwd | 5'-CTTTGCAGCTCTTGATCT-3'          | 57                         |
|               | hSeP15RT-Rev | 5'-CATACAGCTTTTGGTTTCAA-3'        |                            |
| <i>SEPP1</i>  | SePP1RT-Fwd  | 5'-TGCCTTTTTCCTTCCTAACTT-3'       | 55                         |
|               | SePP1RT-Rev  | 5'-CTTCATCTTTGAGAGTCGTGA-3'       |                            |
| <i>SEPW1</i>  | hSePW1RT-Fwd | 5'-AAGTCCAAGTATCTTCAGCTCAAG-3'    | 60                         |
|               | hSePW1RT-Rev | 5'-TCTTCTTAGAGTGAATCAACTTC-3'     |                            |
| <i>SPS2</i>   | hSPS2RT-Fwd  | 5'-GTCCTTTGTTATTCATAATCTGCC-3'    | 60                         |
|               | hSPS2RT-Rev  | 5'-GTTTCAGCTGAGGTTCTTG-3'         |                            |
| <i>TXNRD1</i> | hTR1RT-Fwd   | 5'-GACAGTTCGTACCAATTAAAGTTGAAC-3' | 60                         |
|               | hTR1RT-Rev   | 5'-GCCAGCATCACCGTATTATATTC-3'     |                            |
| <i>TXNRD2</i> | hTR2RT-Fwd   | 5'-CAGCTTCAGGACAGAAAAGTC-3'       | 57                         |
|               | hTR2RT-Rev   | 5'-GCTGACAGCAGAATCTCTTTC-3'       |                            |
| <i>GAPDH</i>  | GAPDHRT-Fwd  | 5'-GTGGTCTCCTCTGACTTCAAC-3'       | 55                         |
|               | GAPDHRT-Rev  | 5'-GTCATACCAGGAAATGAGCTT-3'       |                            |
| <i>UPF1</i>   | Upf1RT-Fwd   | 5'-CAGGGCTACATCTCCATGAGC-3'       | 55                         |
|               | Upf1RT-Rev   | 5'-CAAGGTAAGTGTCTGGGACAG-3'       |                            |

Table S3. Parameter values after fitting the models to the experimental data.

|               | Model 1                |                                         |              | Model 2                |                                         |              |                               | Model 3                 |                                         |              |                               |
|---------------|------------------------|-----------------------------------------|--------------|------------------------|-----------------------------------------|--------------|-------------------------------|-------------------------|-----------------------------------------|--------------|-------------------------------|
| mRNA          | Transcription<br>[1/s] | tRNAsec<br>binding<br>[ml/<br>(mmol*s)] | NMD<br>[1/s] | Transcription<br>[1/s] | tRNAsec<br>binding<br>[ml/<br>(mmol*s)] | NMD<br>[1/s] | Ribosome<br>drop-off<br>[1/s] | Transcripti<br>on [1/s] | tRNAsec<br>binding<br>[ml/<br>(mmol*s)] | NMD<br>[1/s] | Ribosome<br>drop-off<br>[1/s] |
| <i>GPX1</i>   | 1.59e-5                | 1.50e-4                                 | 6.09e-4      | 1.59e-5                | 1.50e-4                                 | 6.09e-4      | 1.64e-6                       | 1.71e-3                 | 7.74e-5                                 | 0.11         | 2.83e-3                       |
| <i>GPX2</i>   | 8.41e-6                | 1e-7**                                  | 1e-7**       | 8.41e-6                | 1e-7**                                  | 1.58e-7      | 60653                         | 8.96e-4                 | 9.73e-3                                 | 3.19         | 92.48                         |
| <i>GPX4</i>   | 2.38e-4                | 5.17e-5                                 | 9.56e-5      | 2.38e-4                | 5.20e-5                                 | 9.63e-5      | 2.59e-3                       | 0.030                   | 4.03e-6                                 | 4.91e-2      | 6.45e-6                       |
| <i>SELH</i>   | 2.38e-4                | 7.11e-5                                 | 3.33e-4      | 2.38e-4                | 7.15e-5                                 | 3.33e-4      | 2.65e-3                       | 0.032                   | 2.52e-5                                 | 0.091        | 2.87e-5                       |
| <i>SELK</i>   | 4.34e-5                | 1**                                     | 6.72e-6      | /                      | /                                       | /            | /                             | /                       | /                                       | /            | /                             |
| <i>SEP15</i>  | 4.98e-6                | 1e-7**                                  | 1e-7**       | /                      | /                                       | /            | /                             | /                       | /                                       | /            | /                             |
| <i>SEPP1</i>  | 6.15e-6                | 5.57e-7                                 | 7.89e-4      | 6.14e-6                | 6.83e-7                                 | 9.66e-4      | 0.097                         | 2.00e-4                 | 4.59e-7                                 | 3.66e-2      | 9.18e-5                       |
| <i>SEPW1</i>  | 9.36e-5                | 1.54e-4                                 | 5.29e-4      | 9.36e-5                | 1.57e-4                                 | 5.38e-4      | 0.035                         | 1.93e-2                 | 6.87e-5                                 | 0.17         | 4.34e-7                       |
| <i>SPS2</i>   | 2.17e-4                | 1e-7**                                  | 1e-7**       | 2.17e-4                | 1e-7**                                  | 1e-7**       | 93129                         | 7.6e-3                  | 1.35e-3                                 | 0.84         | 49.63                         |
| <i>TXNRD1</i> | 8.35e-5                | 1.21e-7                                 | 9.02e-4      | 4.30e-4                | 1.21e-7                                 | 9.16e-3      | 0.020                         | 9.67e-4                 | 1.17e-7                                 | 1.88e-2      | 1.98e-3                       |
| <i>TXNRD2</i> | 1.24e-4                | 3.72e-6                                 | 7.69e-5      | 1.24e-4                | 3.86e-6                                 | 7.98e-5      | 1.85e-3                       | 3.44e-3                 | 3.99e-7                                 | 1.14e-2      | 3.29e-3                       |

\*\* the parameter was not identifiable in the model with the available experimental data