

**Supplementary information**

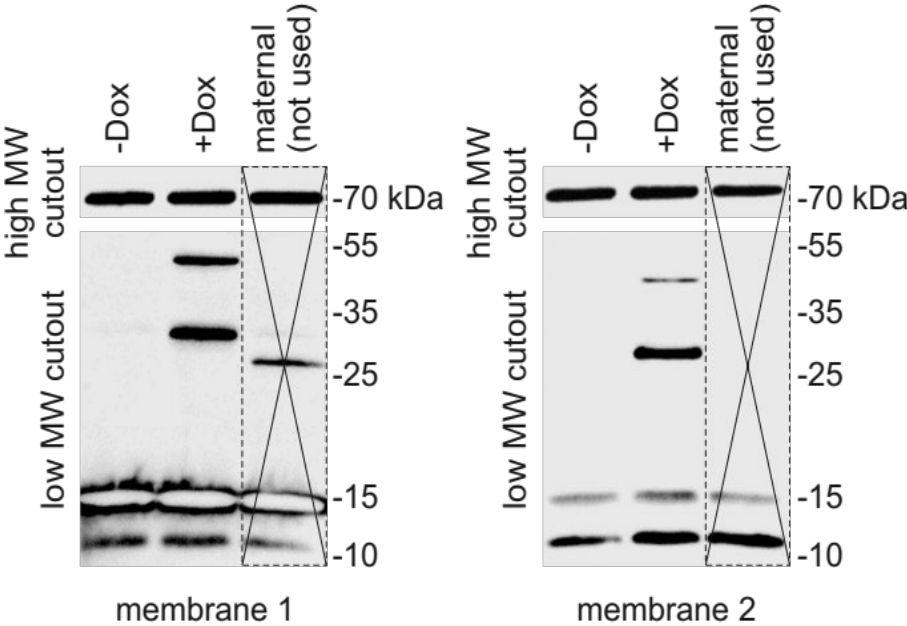
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**Ageing-associated changes in  
transcriptional elongation influence  
longevity**

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In the format provided by the  
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Supplementary Figure 1



**Supplementary Table 1:** Description of the RNA-seq datasets used in the study.

<b>Species</b>	<b>Tissue</b>	<b>Enrichment protocol</b>	<b>Sequencing parameters</b> Paired-/single-end, read length, millions of reads (M)	<b>Time points<sup>1</sup> and conditions</b>
<i>C. elegans</i>	Whole body	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 25 M	Day 1 ( <i>WT</i> ), day 7 ( <i>WT</i> ), day 14 ( <i>WT</i> ), day 21 ( <i>WT</i> )
	Whole body	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 25 M	Day 14 ( <i>WT</i> , <i>daf-2(e1370)</i> , <i>ama-1(m322)</i> )
	Whole Body	TruSeq Stranded Total RNA library	Paired-end, 75 bp, 25 M	Day 1 ( <i>WT</i> , <i>ama-1(m322)</i> )
<i>D. melanogaster</i>	Head	TruSeq Stranded Total RNA Library	Single-end, 100 bp, 37.5 M	Day 30 ( <i>WT</i> , <i>dilp2,3-5</i> ), Day 50 ( <i>WT</i> , <i>dilp2,3-5</i> )
	Head	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 30 M	Day 10 ( <i>WT</i> , <i>RpII215<sup>C4</sup></i> ), day 50 ( <i>WT</i> , <i>RpII215<sup>C4</sup></i> )
<i>M. musculus</i>	Kidney	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 70 M	Month 3 ( <i>WT</i> ), month 24 ( <i>WT</i> )
	Kidney	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 30 M	Month 3 ( <i>WT</i> , <i>DR</i> ) (4 replicates)
	Liver	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 37.5 M	Month 5 ( <i>WT</i> , <i>DR</i> )
	Liver	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 37.5 M	Month 16 ( <i>WT</i> , <i>DR</i> )

<sup>1</sup> Triplicate except where mentioned otherwise.

Species	Tissue	Enrichment protocol	Sequencing parameters Paired-/single-end, read length, millions of reads (M)	Time points <sup>1</sup> and conditions
	Liver	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 37.5 M	Month 27 ( <i>WT</i> , <i>DR</i> )
	Blood	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 70 M	Month 5 ( <i>WT</i> ), month 27 ( <i>WT</i> )
	Hypothalamu s	TruSeq Stranded Total RNA Library	Single-end, 100 bp, 30 M	Month 26 ( <i>WT</i> , <i>IRS1</i> <sup>-/-</sup> )
<i>R. norvegicus</i> (17)	Liver	TruSeq Stranded Total RNA Library	Single-end, 50 bp, 60 M	Month 6 ( <i>WT</i> ), month 24 ( <i>WT</i> ) (2 replicates)
	Brain <sup>2</sup>	TruSeq Stranded Total RNA Library	Single-end, 50 bp, 20 M	Month 6 ( <i>WT</i> ), month 24 ( <i>WT</i> ) (6 replicates)
<i>H. sapiens</i>	Fetal lungs (IMR90)	Nascent RNA	Paired-end, 75 bp, 25 M	Early passage, late passage (2 replicates)
	Fetal lungs (IMR90)	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 50 M	Early passage, late passage (2 replicates)
	Umbilical vein endothelial (HUVECs)	Nascent RNA	Paired-end, 75 bp, 50 M	Early passage, late passage (2 replicates)
	Umbilical vein endothelial (HUVECs)	TruSeq Stranded Total RNA Library	Paired-end, 75 bp, 100 M	Early passage, late passage

<sup>2</sup> Not included in the analysis due to low coverage (bellow 1X genome coverage or 29 M sequenced reads for *R. norvegicus* ; genome coverage calculated using Lander-Waterman formula)

<b>Species</b>	<b>Tissue</b>	<b>Enrichment protocol</b>	<b>Sequencing parameters</b> Paired-/single-end, read length, millions of reads (M)	<b>Time points<sup>1</sup> and conditions</b>
	Fibroblast skin	TruSeq Stranded Total RNA Library	Paired-end, 100 <i>bp</i> , 100 M	Progeria patient (HSS) (2 replicates)
			Paired-end, 75 <i>bp</i> , 100 M	Healthy donor, sex/age matched with progeria patient (2 replicates)
	Blood	TruSeq Stranded Total RNA Library	Paired-end, 75 <i>bp</i> , 70 M	Healthy donor, 6 females, 6 males, age range: 21-70

**Supplementary Table 2:** Pearson correlations between the change in elongation rate and characteristics of the introns in which the elongation rate was measured in the respective RNA-Seq datasets

<b>Species</b>	<b>Comparison</b>	<b>Distance from promoter</b>	<b>Intron length</b>	<b>Gene expression log2FC</b>	<b>Circular RNA index</b>
<i>C. elegans</i>	21 d vs 1 d	0.014	0.071	-0.266	-0.085
<i>C. elegans</i>	14 d ama-1 vs 14 d wt	0.008	-0.110	-0.247	0.160
<i>C. elegans</i>	14 d daf2 vs 14 d wt	0.020	0.007	-0.278	0.130
<i>D. melanogaster</i>	50 d vs 10 d	-0.036	0.019	-0.023	0.019
<i>D. melanogaster</i>	50 d RpII215 vs 50 d	0.002	-0.091	-0.161	-0.043
<i>D. melanogaster</i>	50 d dilp 2,3-5 vs 50 d	-0.133	-0.170	0.041	-0.092
<i>M. musculus</i>	24 mo vs 3.5 mo	0.011	0.043	-0.230	-0.045
<i>H. sapiens</i>	Senescent vs proliferating (IMR90)	-0.021	0.046	-0.274	0.184
<i>H. sapiens</i>	Senescent vs proliferating (HUVEC)	0.014	0.036	-0.289	0.020

**Supplementary Table 3:** Sample size of statistical comparisons in the main figures.

Species	Comparison	Fig. 1c/ Fig. 2a (All introns)	Fig. 1c/ Fig. 2a (Consistent introns)	Fig. 3a	Fig. 3b	Fig. 3c	Fig. 3d (Genes)
<i>C. elegans</i>	14 d vs 1 d	576	115	2701	335	7096	5752
<i>C. elegans</i>	21 d vs 1 d	520	129	2451	335	7096	5752
<i>C. elegans</i>	14 d ama-1 vs 14 d wt	594	176	2404	3702	5849	6238
<i>C. elegans</i>	1 d ama-1 vs 1 d wt	557	99	-	3702	-	6238
<i>C. elegans</i>	14 d wt vs 1 d wt	436	107	-	-	-	6238
<i>C. elegans</i>	14 d daf2 vs 14 d wt	518	69	2257	3702	-	6238
<i>D. melanogaster</i>	50 d vs 30 d	531	78	-	120	-	-
<i>D. melanogaster</i>	50 d RpII215 vs 50 d	1233	257	1638	2653	4952	2727
<i>D. melanogaster</i>	10 d RpII215 vs 10 d	1297	374	-	2653	4952	2727
<i>D. melanogaster</i>	50 d RpII215 vs 10 d RpII215	1316	299	-	2653	-	
<i>D. melanogaster</i>	50 d wt vs 10 d wt	1200	209	1676	2653	4952	
<i>D. melanogaster</i>	10 d dilp 2,3- 5 vs 10 d	546	77	-	120	-	-
<i>D. melanogaster</i>	50 d dilp 2,3- 5 vs 50 d	527	153	-	120	-	-
<i>M. musculus</i>	Blood (Old vs. young)	1559	152	4546	393	41004	1950
<i>M. musculus</i>	DR (5 weeks)	3280	625	-	-	-	3441

Species	Comparison	Fig. 1c/ Fig. 2a (All introns)	Fig. 1c/ Fig. 2a (Consistent introns)	Fig. 3a	Fig. 3b	Fig. 3c	Fig. 3d (Genes)
<i>M. musculus</i>	DR (16 weeks)	3636	609	-	-	-	3441
<i>M. musculus</i>	DR (26 weeks)	3586	629	-	-	-	3441
<i>M. musculus</i>	Caloric restriction, kidney	3270	148	-	1952	-	2171
<i>M. musculus</i>	24 mo vs 3.5 mo	4455	597	1457	2486	13297	5674
<i>M. musculus</i>	26 mo IRS vs 26 mo	5555	390	711	2200	-	-
<i>R. norvegicus</i>	24 mo vs. 6 mo	6384	2095	376	-	-	-
<i>H. sapiens</i>	Blood (Old vs. young)	6746	57	6120	2166	28683	4969
<i>H. sapiens</i>	Senescent vs Proliferating (IMR90)	6969	2988	773	4932	1121	3403
<i>H. sapiens</i>	Senescent vs Proliferating (HUVEC)	6497	741	8486	6283	26701	8620