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Supplementary Table 1: List of primers used in PCR analysis[1]

Number	Designation	Sequence	Notes
Primer set 1	MDL15UTRPRAF MDL15UTRPRAR Amplicon A, Fig. 1b	GCCAAGATGGCCGAATAGGA AAATCACCCGTCTTCTGCGT	LINE-1 5'UTR, positions 12-31, sense orientation[2]. LINE-1 5'UTR, positions 64-83, antisense orientation[2]. Used in RT-qPCR experiments to assess expression of L1Hs RNA. Also used in ChIP experiments.
Primer set 2	MDL15UTRBF MDL15UTRBR Amplicon B, Fig. 1b	CGAGATCAAACTGCAAGGCG CCGGCCGCTTTGTTTACCTA	LINE-1 5'UTR, positions 402-421, sense orientation[2]. LINE-1 5'UTR, positions 454-473, antisense orientation[2]. Used in RT-qPCR experiments to assess expression of L1Hs RNA. Also used in ChIP experiments.
Primer set 3	MDL15UTRCF MDL15UTRCR Amplicon C, Fig. 1b	TAAACAAAGCGGCCGGGAA AGAGGTGGAGCCTACAGAGG	LINE-1 5'UTR, positions 474-492, sense orientation[2]. LINE-1 5'UTR, positions 530-549, antisense orientation[2]. Used in RT-qPCR experiments to assess expression of L1Hs RNA. Also used in ChIP experiments.
Primer set 4	MDL15UTRDF MDL15UTRDR Amplicon D, Fig. 1b	AGAGAGCAGTGGTTCTCCCA CAGTCTGCCCGTTCTCAGAT	LINE-1 5'UTR, positions 619-638, sense orientation[2]. LINE-1 5'UTR, positions 647-666, antisense orientation[2]. Used in RT-qPCR experiments to assess expression of L1Hs RNA. Also used in ChIP experiments.
Primer set 5	MDL1ORF1F MDL1ORF1R Amplicon E, Fig. 1b	ACCTGAAAGTGACGGGGAGA CCTGCCTTGCTAGATTGGGG	LINE-1 ORF1, positions 1395-1414, sense orientation[2]. LINE-1 ORF1, positions 1508-1527, antisense orientation[2]. Used in RT-qPCR experiments to assess expression of L1Hs RNA. Also used in ChIP experiments.
Primer set 6	ORF2F ORF2R ORF2 probe Amplicon F, Fig. 1b	CAAACACCGCATATTCTCACTCA CTTCCTGTGTCCATGTGATCTCA AGGTGGGAATTGAAC-VIC	LINE-1 ORF2, positions 5731-5753, sense orientation[2]. LINE-1 ORF2, positions 5772-5794, antisense orientation[2]. Probe for TaqMan experiments. ORF2F and ORF2R were used in SYBR Green RT-qPCR experiments to assess expression of L1Hs RNA, and in conjunction with the ORF2 probe in TaqMan qPCR experiments on genomic DNA to determine relative copy numbers of L1Hs elements. Primers were developed and validated as described[3].
Primer set 7	5SF 5SR 5S probe	CTCGTCTGATCTCGGAAGCTAAG GCGGTCTCCCATCCAAGTAC AGGGTCGGGCCTGG-6FAM	Ribosomal 5S RNA gene, sense orientation. Ribosomal 5S RNA gene, antisense orientation. Probe for TaqMan experiments. Used for internal normalization, in conjunction with primer set 3, in TaqMan qPCR experiments on genomic DNA to determine relative copy numbers of L1Hs elements. Primers were developed and validated as described[3].
Primer set 8	GAPDHFW GAPDHRV	TTGAGGTCAATGAAGGGGTC GAAGGTGAAGGTCGGAGTCA	*GAPDH*, sense orientation. *GAPDH*, antisense orientation. Used for RT-qPCR of the mRNA of the *GAPDH* gene (NM_001256799). Primers span an intron. Used as the internal normalizer in gene expression experiments.
Primer set 9	GAPDHINT4F GAPDHINT4R	CCAGGAGTGAGTGGAAGACAG CTAGTTGCCTCCCCAAAGCA	Intron 4 of *GAPDH*, sense orientation. Intron 4 of *GAPDH*, antisense orientation. Used as a negative control in ChIP experiments.
Primer set 10	ACP1IFNAFW ACP1IFNARV1 ACP1IFNARV2	TTGATGGCAACCAGTTCCAG TCATCCCAAGCAGCAGATGA TGTTCCCAAGCAGCAGATGA	Interferon alpha consensus, sense orientation. Interferon alpha consensus, antisense orientation. Interferon alpha consensus, antisense orientation. Used in RT-qPCR experiments to assess the collective expression of human interferon alpha genes. All 3 primers were used in a single reaction.
Primer set 11	MDIFNB1FW MDIFNB1RV	ACGCCGCATTGACCATCTAT GTCTCATTCCAGCCAGTGCT	*IFNB1*, sense orientation. *IFNB1*, antisense orientation.

			Used for RT-qPCR of the mRNA of the *IFNB1* gene (NM_002176).
Primer set 12	MDHSRB1AF MDHSRB1AR	ACTCTCACCTCCCATGTTGC ATCCGTGCACTCCTGTTCTG	*RB1*, sense orientation. *RB1*, antisense orientation. Used for RT-qPCR of the mRNA of the *RB1* gene (NM_000321). Primers span an intron.
Primer set 13	MDHSP107AF MDHSP107AR	CCAAGAAGCGCTCTGCTGTA GCAGGGGATTCTGCATCACTA	*RBL1*, sense orientation. *RBL1*, antisense orientation. Used for RT-qPCR of the mRNA of the *RBL1* gene (NM_0028955). Primers span an intron.
Primer set 14	MDHSP130F MDHSP130R	AGTCGCCCACCCCTCAGAT TTCCCTCCAGCGTGTAGCTT	*RBL2*, sense orientation. *RBL2*, antisense orientation. Used for RT-qPCR of the mRNA of the *RBL2* gene (NM_005611). Primers span an intron.
Primer set 15	MDTREX1CDSF MDTREX1CDSR	TCCCCTTCGGATCTTAACAC CGAAAAAGATGAGGGTCTGC	*TREX1*, sense orientation. *TREX1*, antisense orientation. Used for RT-qPCR of the mRNA of the *TREX1* gene (NM_007248). Primers span an intron.
Primer set 16	MDHSFOXA1F MDHSFOXA1R	GGAAGACCGGCCAGCTAGAG TGAAGGAGTAGTGGGGGTCC	*FOXA1*, sense orientation. *FOXA1*, antisense orientation. Used for RT-qPCR of the mRNA of the *FOXA1* gene (NM_004496). Primers span an intron.
Primer set 17	JJMMP1FW JJMMP1RV	AGCCTTCCAACTCTGGAGTAATGT CCGATGATCTCCCCTGACAA	*MMP1*, sense orientation. *MMP1*, antisense orientation. Used for RT-qPCR of the mRNA of the *MMP1* gene (NM_001145938). Primers span an intron.
Primer set 18	JJMMP3FW JJMMP3RV	CCCACCTTACATACAGGATTGTGA CCCAGACTTTCAGAGCTTTCTCA	*MMP3*, sense orientation. *MMP3*, antisense orientation. Used for RT-qPCR of the mRNA of the *MMP3* gene (NM_002422). Primers span an intron.
Primer set 19	JJIL6FW JJIL6RV	CACTGGCAGAAAACAACCTGAA ACCAGGCAAGTCTCCTCATTGA	*IL6*, sense orientation. *IL6*, antisense orientation. Used for RT-qPCR of the mRNA of the *IL6* gene (NM_000600). Primers span an intron.
Primer set 20	JJIL8FW JJIL8RV	GTTTTTGAAGAGGGCTGAGAATTC CCCTACAACAGACCCACACAATAC	*CXCL8 (IL8)*, sense orientation. *CXCL8 (IL8)*, antisense orientation. Used for RT-qPCR of the mRNA of the *CXCL8* gene (NM_000584). Primers span an intron.
Primer set 21	JJCCL2FW JJCCL2RV	AAGACCATTGTGGCCAAGGA TTCGGAGTTTGGGTTTGCT	*CCL2*, sense orientation. *CCL2*, antisense orientation. Used for RT-qPCR of the mRNA of the *CCL2* gene (NM_002982). Primers span an intron.
Primer set 22	JJCXCL2FW JJCXCL2RV	AGAATGGGCAGAAAGCTTGTCT CCTTCTGGTCAGTTGGATTTGC	*CXCL2*, sense orientation. *CXCL2*, antisense orientation. Used for RT-qPCR of the mRNA of the *CXCL2* gene (NM_002089). Primers span an intron.
Primer set 23	IL1BETAFW IL1BETARV	CGCCAGTGAAATGATGGCTTAT CTGGAAGGAGCACTTCATCTGT	*IL-1β,* sense orientation. *IL-1β,* antisense orientation. Used for RT-qPCR of the mRNA of the *IL1B* gene (NM_000576). Primers span an intron
Primer set 24	MDIRF9FW MDIRF9RV	CAACTGAGGCCCCCTTTCAA CGCCCGTTGTAGATGAAGGT	*IRF9,* sense orientation. *IRF9,* antisense orientation. Used for RT-qPCR of the mRNA of the *IRF9* gene (NM_006084). Primers span an intron
Primer set 25	MDIRF7FW	GGCTGGAAAACCAACTTCCG	*IRF7,* sense orientation.

	MDIRF7RV	GTTATCCCGCAGCATCACGA	*IRF7,* antisense orientation. Used for RT-qPCR of the mRNA of the *IRF7* gene (NM_001572). Primers span an intron
Primer set 26	MDHSOAS1AF MDHSOAS1AR	TGGAGACCCAAAGGGTTGGA AGGAAGCAGGAGGTCTCACC	*OAS1,* sense orientation. *OAS1,* antisense orientation. Used for RT-qPCR of the mRNA of the *OAS1* gene (NM_016816). Primers span an intron
Primer set 27	HSCGASFW HSCGASRV	ACGTGCTGTGAAAACAAAGAAG GTCCCACTGACTGTCTTGAGG	*cGAS,* sense orientation. *cGAS,* antisense orientation. Used for RT-qPCR of the mRNA of the *MB21D1* gene (NM_138441). Primers span an intron
Primer set 28	HSSTING1FW HSSTING1RV	ATATCTGCGGCTGATCCTGC GGTCTGCTGGGGCAGTTTAT	*STING,* sense orientation. *STING,* antisense orientation. Used for RT-qPCR of the mRNA of the *TMEM173* gene (NM_198282). Primers span an intron
Primer set 29	TICDKN1AFW TICDKN1ARV	GAGACTCTCAGGGTCGAAAACG TTCCTGTGGGCGGATTAGG	*CDKN1A,* sense orientation. *CDKN1A,* antisense orientation. Used for RT-qPCR of the mRNA of the *CDKN1A* gene (NM_000389). Primers span an intron
Primer set 30	TICDKN2AFW TICDKN2ARV	CGGAAGGTCCCTCAGACATC CCCTGTAGGACCTTCGGTGA	*CDKN2A (p16),* sense orientation. *CDKN2A (p16),* antisense orientation. Used for RT-qPCR of the mRNA of the CDKN2A gene (NM_000077). Primers span an intron
Primer set 31	MGAPDHF MGAPDHR	CGGCCGCATCTTCTTGTG GTGACCAGGCGCCCAATA	*Gapdh,* sense orientation. *Gapdh,* antisense orientation. Used for RT-qPCR of the mRNA of the *Gapdh* gene (NM_008084.3). Primers span an intron. Used as the internal normalizer in gene expression experiments.
Primer set 32	MMHSP90AB1F MMHSP90AB1R	CCACCACCCTGCTCTGTACTA CCTCTCCATGGTGCACTTCC	*Hsp90ab1,* sense orientation. *Hsp90ab1,* antisense orientation. Used for RT-qPCR of the mRNA of the *Hsp90ab1* gene (NM_008302). Primers span an intron. Used as secondary normalizer in gene expression experiments.
Primer set 33	MMGUSBFW MMGUSBRV	CGTGACCTTTGTGAGCAACG CTGCTCCATACTCGCTCTGG	*Gusb,* sense orientation. *Gusb,* antisense orientation. Used for RT-qPCR of the mRNA of the *Gusb* gene (NM_010368). Primers span an intron. Used as secondary normalizer in gene expression experiments.
Primer set 34	GBCONIFNAF GBCONIFNAR	TCTGATGCAGCAGGTGGG AGGGCTCTCCAGACTTCTGCTCT G	Interferon alpha consensus, sense orientation. Interferon alpha consensus, antisense orientation. Used in RT-qPCR experiments to assess the collective expression of murine interferon alpha genes. Primers were developed and validated as described[4].
Primer set 35	GBIRF7FW GBIRF7RV	CTCCTGAGCGCAGCCTTG GTTCTTACTGCTGGGGCCAT	*Irf7,* sense orientation. *Irf7,* antisense orientation. Used for RT-qPCR of the mRNA of the *Irf7* gene (NM_016850). Primers span an intron.
Primer set 36	MMOAS1BF MMOAS1BR	TCTGCTTTATGGGGCTTCGG TCGACTCCCATACTCCCAGG	*Oas1,* sense orientation. *Oas1,* antisense orientation. Used for RT-qPCR of the mRNA of the *Irf9* gene (NM_001083925). Primers span an intron.
Primer set 37	JKLINE1FW JKLINE1RV Amplicon W, Ext. Data Fig. 6f.	CTGCCTTGCAAGAAGAGAGC AGTGCTGCGTTCTGATGATG	Murine LINE-1 5'UTR, positions 392-412, sense orientation. Murine LINE-1 5'UTR, 596-616, antisense orientation. Used in RT-qPCR experiments to assess expression of murine L1 RNA.
Primer set 38	P16MouseF P16MouseR	CCAGGGCCGTGTGCAT TACGTGAACGTTGCCCATCA	*Cdkn2a,* sense orientation. *Cdkn2a,* antisense orientation.

			Used for RT-qPCR of the mRNA of the *Cdkn2*a gene (NM_009877). Primers span an intron.
Primer set 39	GBMMP3FW GBMMP3RV	GACTCAAGGGTGGATGCTGT CCAACTGCGAAGATCCACTG	*Mmp3,* sense orientation. *Mmp3,* antisense orientation. Used for RT-qPCR of the mRNA of the *Mmp3* gene (NM_0108209). Primers span an intron.
Primer set 40	GBIL6FW GBIL6RV	CGGAGAGGAGACTTCACAGAGG A TTTCCACGATTTCCCAGAGAACA	*Il-6,* sense orientation. *Il-6,* antisense orientation. Used for RT-qPCR of the mRNA of the *Il6* gene (NM_031168). Primers span an intron.
Primer set 41	MMPAI1FW MMPAI1RV	GGAAGGGCAACATGACCAGG AGCTGCTCTTGGTCGGAAAG	*Pai1,* sense orientation. *Pai1,* antisense orientation. Used for RT-qPCR of the mRNA of the *Pai1* gene (NM_008871). Primers span an intron.
Primer set 42	APACACAF APACACAR	CTGGCTGCATCCATTATGTCA TGGTAGACTGCCCGTGTGAA	*Acaca,* sense orientation. *Acaca,* antisense orientation. Used for RT-qPCR of the mRNA of the *Acaca* gene (NM_133360). Primers span an intron.
Primer set 43	APFASNF APFASNR	CTGCGTGGCTATGATTATGG AGGTTGCTGTCGTCTGTAGT	*Fasn,* sense orientation. *Fasn,* antisense orientation. Used for RT-qPCR of the mRNA of the *Fasn* gene (NM_007988). Primers span an intron.
Primer set 44	APSREBF1F APSREBF1R	ACTTTTCCTTAACGTGGGCCT CATCTCGGCCAGTGTCTGTT	*Srebf1,* sense orientation. *Srebf1,* antisense orientation. Used for RT-qPCR of the mRNA of the *Srebf1* gene (NM_011480). Primers span an intron.
Primer set 45	APCEBPAF APCEBPAR	TTCGGGTCGCTGGATCTCTA TCAAGGAGAAACCACCACGG	*C/EBPα,* sense orientation. *C/EBPα,* antisense orientation. Used for RT-qPCR of the mRNA of the *C/EBPα* gene (NM_007678).
Primer set 46	APACACBF APACACBR	AGAAGCGAGCACTGCAAGGTTG GGAAGATGGACTCCACCTGGTT	*Acacb,* sense orientation. *Acacb,* antisense orientation. Used for RT-qPCR of the mRNA of the *Acacb* gene (NM_133904). Primers span an intron.
Primer set 47	APPPARGF APPPARGR	TTCGCTGATGCACTGCCTAT GGAATGCGAGTGGTCTTCCA	*Pparg,* sense orientation. *Pparg,* antisense orientation. Used for RT-qPCR of the mRNA of the *Pparg* gene (NM_011146). Primers span an intron.
Primer set 48	MDMML1ORF1F MDMML1ORF1R Amplicon X, Ext. Data Fig. 6f.	ATCTGTCTCCCAGGTCTGCT TCCTCCGTTTACCTTTCGCC	Murine LINE-1 ORF1, positions 1341-1360, sense orientation. Murine LINE-1 ORF1, positions 1460-1441, antisense orientation. Used in RT-qPCR experiments to assess expression of murine L1 RNA.
Primer set 49	MDMML1ORF2F MDMML1ORF2R Amplicon Y, Ext. Data Fig. 6f.	GCTTCGGTGAAGTAGCTGGA TTCGTTAGAGTCACGCCGAG	Murine LINE-1 ORF2, positions 4786-4805, sense orientation. Murine LINE-1 ORF2, positions 4939-4920, antisense orientation. Used in RT-qPCR experiments to assess expression of murine L1 RNA.
Primer set 50	MDMML13UTRF MDMML13UTRR Amplicon Z, Ext. Data Fig. 6f.	AGCCAAATGGATGGACCTGG AAGGAGGGGCATAGTGTCCA	Murine LINE-1 3'UTR, positions 6344-6363, sense orientation. Murine LINE-1 3'UTR, positions 6538-6519, antisense orientation. Used in RT-qPCR experiments to assess expression of murine L1 RNA.
Primer set 51	MDMML1TFF MDMML1TFR	ATCCGGACCAGAGGACAGG ATGGCGACCGCTGCTG	Murine LINE-1 5'UTR sense orientation. Murine LINE-1 5'UTR, antisense orientation. Primers amplify one of the polymorphisms of L1Tf(I-III) families.

Primer set 52	MDMML1MDNF MDMML1MDNR	AGAGAACCGGACCCAATCCA GCTTGTGCCCCTACTCAGAC	Murine LINE-1 5'UTR sense orientation. Murine LINE-1 5'UTR, antisense orientation. Primers amplify one of the polymorphisms of L1MdN(I) families.
Primer set 53	MDMML1MDAF MDMML1MDAF	TCCCCACGGGATCCTAAGAC CTCTGCAGGCAAGCTCTCTT	Murine LINE-1 5'UTR sense orientation. Murine LINE-1 5'UTR, antisense orientation. Primers amplify one of the polymorphisms of L1MdA(IV-VII) families.

[1] All sequences are listed in the 5'->3' orientation. Primer sets 1–30 are specific for the listed human genes; primer sets 31–53 are murine-specific.
[2] All LINE-1 positions are relative to the L1Hs consensus sequence (Repbase, http://www.girinst.org/repbase/).
[3] See reference #16 (Coufal *et al*., 2009).
[4] See reference #41 (Gautier *et al*., 2005).

Supplementary Table 2: List of antibodies

Antibody	Antibody species	Vendor	Catalog Number	Application
GAPDH	Rabbit	Cell Signaling	5174	Loading control for immunoblotting
GAPDH	Mouse	Sigma	G8795	Loading control for immunoblotting
p16	Mouse	Santa Cruz	sc-756	Immunoblotting
p16	Mouse	Santa Cruz	sc-56330 (JC8)	Immunofluorescence
p21	Rabbit	Santa Cruz	sc-397	Immunoblotting
RB1	Mouse	BD Biosciences	554136	Immunoblotting, ChIP
TREX1	Rabbit	Cell Signaling	12215	Immunoblotting
FOXA1	Rabbit	Abcam	ab170933	Immunoblotting
FOXA1	Goat	Abcam	ab5089	ChIP
Phospho-STAT1 (Tyr701)	Mouse	Santa Cruz	sc-8394	Immunofluorescence
Phospho-STAT2 (Tyr689)	Mouse	Millipore	07-224	Immunofluorescence
STAT2	Rabbit	Cell Signaling	4594S	Immunoblotting
IRF7	Rabbit	Abcam	ab109255	Immunoblotting
IRF9	Rabbit	Novus Bio	NBP2-16991	Immunofluorescence
BrdU	Mouse	BD Biosciences	555627	Immunofluorescence
γ-H2AX	Mouse	Millipore	05-636	Immunofluorescence
F4/80	Rat	Abcam	ab6640 (CI:A3-1)	Immunofluorescence
ssDNA	Mouse	Enzo	MAb F7-26	Immunofluorescence
DNA-RNA hybrids	Mouse	Kerafast	ENH001 (S9.6)	Immunofluorescence
LaminB1	Goat	Santa Cruz	Sc-6216 (C-20)	Immunofluorescence
IL-6	Rabbit	Cell Signaling	12912	Immunofluorescence
Human LINE-1 ORF1	Rabbit	Gift of K.H. Burns, Johns Hopkins[1]		Immunofluorescence
Mouse LINE-1 Orf1	Rabbit	J.D. Boeke, abEA02 (RabMAb clone NYU-2-1_2		Immunofluorescence

[1] See reference #4

Supplementary Table 3: List of expressed L1 elements identified by long range RT-PCR

See Excel file: Table_S3.xlsx

Supplementary Table 4a: Gene list used in GSEA for SASP (85 genes)
Supplementary Table 4b: Gene list used in GSEA for IFN-I (50 genes)

See Excel file: Table_S4.xlsx

Supplementary Table 5a: GSEA analysis of KEGG pathways comparing early passage with early senescence
Supplementary Table 5b: GSEA analysis of KEGG pathways comparing early passage with late senescence
Supplementary Table 5c: GSEA analysis of KEGG pathways comparing early senescence with late senescence

See Excel file: Table_S5.xlsx

Supplementary Table 6: Summary of Qiagen PCR array analysis

	SEN (L) cells		3X cells	
	Number of genes	Percent[1]	Number of genes	Percent[1]
Total genes	84	100%	84	100%
Upregulated genes	77	92%	80	95%
Downregulated genes	7	8%	4	5%
Changing genes passing filters[2]	58	69%	44	52%
Passing genes upregulated	57	68%	44	52%
Passing genes downregulated	1	1%	0	0%
Changing genes failing filters	26	31%	40	48%
Genes passing filters, unique[3]	23	27%	9	11%
Genes passing filters, overlap[4]	35	42%	35	42%
Genes passing filters, total[5]	67	80%	67	80%

[1] All percentages are calculated with respect to the total number of genes (84) found on the array. Data for all 84 genes displayed as scatter plots are shown in Fig. 2h.

[2] The sum of upregulated and downregulated genes that pass a set of significance filters, see Methods for definitions of filters.

[3] Changing genes that pass the significance filters that are unique to either SEN (L) or 3X cells.

[4] Changing genes that pass the significance filters that are common to (found in both) SEN (L) and 3X cells.

[5] Changing genes that pass the significance filters that are found in SEN (L) and/or 3X cells. The heatmap representation for this set of genes (67) is shown in Extended Fig. 4j, k.

Supplementary Table 7: Summary of mouse tissue RT-qPCR data for L1, p16, IFN-I and SASP genes

See Excel file: Table_S7.xlsx