Supplemental Table 1. Characteristics of Model Systems for the Study of Pathway of Cellular Senescence and Immortalization

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
Human diploid fibroblast cell line from a patient with Werner Syndrome (WS8) undergoing premature senescence	Differential screening of a cDNA library	Overexpressed in senescent cells: *COL1α1 (α1(I)procollagen)* *COL1α2 (α2(I)procollagen)* *Ferritin heavy chain* *Fibronectin* *IGFBP3* *Osteonectin* *PAI-1* *Thrombospondin* *αB−crystallin* 9 unknown	Cell cycle Cytoskeleton IGF		(Murano et al., 1991)
Young and senescent human diploid fibroblast (HDF) cell lines, BJ and IMR90	Enhanced differential display	7 known genes and 6 novel genes upregulated in old HDF *CD44* *SOD* *HEREGULIN* *HTF (F3)* *IFNγ* *IGFPB5* *PAI-2* 5 known genes and 5 novel genes downregulated in old HDF *80K-L* *ALDH-1* *LAMININA* *COL1α1* *COL3α1*	Cell adhesion Cell cycle Cytoskeleton IGF MAP kinase Oxidative stress		(Linskens et al., 1995)
Human diploid fibroblast cell line from a patient with Werner Syndrome (WS8) undergoing premature senescence	Subtractive WS cDNA library	Overexpressed in senescent cells: *Acid sphingomyelinase* *EF-1α* *EIF-2β* *Fibronectin* *nm23-H2* *Osteonectin* *10 unknown clones*	Cell adhesion Cell cycle Cytoskeleton		(Lecka-Czernik et al., 1996)
Spontaneously immortalized LFS cell lines: MDAH041 and MDAH087	(1) 5-aza-dC treatment (2) Infection of cells with retrovirus encoding gene of interest	$p16^{INK4a}$ $p21^{CIP1/WAF1}$	Cell cycle	Senescent morphology[a] SA β-gal assay Inhibits cell growth	(Vogt et al., 1998)
Primary keratinocytes	Overexpression of ID1	ID1	Cell cycle	Overexpression leads to immortalization; assessed by population doubling ID1 overexpression results in an increase in pRB phosphorylation ID1 elevates expression of hTERT and increases telomerase activity	(Alani et al., 1999)

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
Human fibroblast cell line BJ, human retinal pigment cell line RPE 340, and human umbilical vein endothelial cell line (HUVEC)	cDNA microarrays of approximately 1,000 genes	Senescence gene expression profile is cell lineage dependent			(Shelton et al., 1999)
Id1-wt MEF Id1-null MEF	Growth of wt and null Id1 MEF	ID1	Cell cycle	Id1-null MEF exhibit premature senescence Senescent morphology[a] SA β-gal assay	(Alani et al., 2001)
Cervical tumor cell line HeLa S3 and human embryonic lung fibroblast TIG-7	Subtractive cDNA library BrdU treated and untreated Hela and differential colony hybridization	*26 genes and 11 ESTs with increased expression during senescence including:* *Collagenase I* *Fibronectin* *IGFBP3* *IGFBP4* *p21$^{CIP1/WAF1}$* *PAI-1*	Cell cycle Cytoskeleton		(Suzuki et al., 2001)
MCF-7 human breast carcinoma cell line	IGFBPrP1 overexpressed	*IGFBPrP1*	Cell cycle IGF	Cell counts show expression suppresses proliferation Quantitation noncycling cells by BrdUrd-Hoechst flow cytometry SA β-gal assay Senescent morphology[a]	(Wilson et al., 2002)
Effects of 5-aza-dC on human fibroblast cell line, LD419 and human bladder tumor cell line, T24	Affymetrix oligonucleotide microarray containing 6,600 genes	A cutoff fold change of > or < 4-fold was used to identification of genes up- and downregulated following 8 days 5-aza-dC treatment LD419 cells 34 genes upregulated (10 inducible by IFN) including *STAT1* 11 genes downregulated T24 cells 61 genes upregulated (33 inducible by IFN) including *IRF7, PAI-2, STAT1 and TNFAIP3* 2 genes downregulated	Cell cycle IFN pathway Tumor antigens		(Liang et al., 2002)
Human prostate epithelial cells (HPECs) passage to senescence and HPV16 E7 immortalized HPECs	cDNA microarray about 20,000 unique genes and ESTs	Genes that were upregulated in senescence and downregulated in immortalization: *IGFBP3* *BRAK* *DOC1* 93 genes (51 known function) upregulated in senescence	 Cytokine Cytoskeleton		(Schwarze et al., 2002)

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
		including: *IGFBP2* *Fibronectin* *MDM2* *RhoB* *p16^{INK4a}* *p21$^{CIP1/WAF1}$* 159 genes (77 known function) downregulated in senescence	Differentiation ECM Growth regulator/tumor association IGF Motility/migration Stress/injury/xenobiotic Transcription		
		137 genes (70 known function) downregulated in immortalization including: *AhR* *IGFBP5* *IGFBPrP2 (CTGF)* *Osteonectin* 92 genes (40 known function) upregulated in immortalization	Cell adhesion Cell cycle Cytoskeleton ECM IGF Signaling/growth/ cytokine Calcium regulation Stress/xenobiotic		
Spontaneous and chemically immortalized human fibroblast and keratinocyte cell lines Immortalized cell lines telomere length was maintained by ALT or telomerase	Analysis mRNA, and protein expression, and CpG island methylation	Association of genes with immortalization p16^{INK4a} pRB	Cell cycle	p16^{INK4a}: little to no expression at mRNA or protein level. pRB: hyperphosphorylated	(Tsutsui et al., 2002)
Prostate epithelial cells	SAGE, SAGE tags represented 25,645 unique mRNA species	A cutoff of $P < 0.05$ and fold changed > 2.5 was used for identification of up- and downregulated genes			(Untergasser et al., 2002)
		157 mRNAs (70 known genes) upregulated during senescence including: *Cyclin D1* *Fibronectin* *Gelsolin* *PAI-1* *RAC1* *Vimentin* *4 IFN related genes* 116 mRNAs (65 known genes) repressed during senescence including: *CKS1* *Cyclin B1* *E2F4* *EGR1* *ID1*	Actin fragmentation Cell adhesion Cell cycle ECM remodeling IFN Intermediate filament Lamellipodia formation G_2-M regulation Transcription factor		

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
Rapidly proliferating (PD12) and senescent (PD19) normal human oral keratinocytes	Human ExpressChip HO1, HO2 and HO3, representing 3,195 annotated genes	Approximately 5% of the 3195 screened genes were upregulated 3 to 500-fold in senescent cells including: *$p16^{INK4a}$* *$p15^{INK4b}$* *$p19^{INK4d}$* *p57* *CYP1B1* *COL1α1* *Fibronectin* *IGFBP3* *IGFBPrP2 (CTGF)*	Cell cyclin dependent kinase inhibitors Apolipids ECM Mitochondrial proteins		(Kang et al., 2003)
Precrisis, spontaneously immortalized and 5-aza-dC treated immortalized LFS cell line: MDAH041	Affymetrix HGU95Av2 oligonucleotide microarray Spontaneously immortalized MDAH041 LFS fibroblasts were compared to precrisis LFS fibroblasts and to 5-aza-dC treated immortalized LFS cells	Expression of 85 genes decreased during immortalization and increased following 5-aza-dC treatment 39 of the 85 genes were IFN pathway regulated genes	IFN		(Kulaeva et al., 2003)
Murine bone marrow	Dimerized form of MLL	MLL	Apoptosis Cell cycle Transcription	Growth Morphology Cell cycle analysis	(Martin et al., 2003)
HeLa cells infected with empty adenovirus vector or E2 containing adenovirus vector (in order to induce senescence)	Affymetrix HGU95Av2 oligonucleotide microarray	Genes upregulated senescence *$p21^{CIP1/WAF1}$* *p57* *p130* *Cyclin G2* *RAB2L* *RAB5B* *RAB13* *RAB31* *RAB1F* *RABGGTA*	G1/S Arrest Vesicular transport		(Wells et al., 2003)
Human prostate epithelial cancer cell lines DU-145 (nonfunctional pRB and p53), PC-3 (functional pRB, mutant p53), and LNCaP (functional pRB and p53)	Overexpression of IFI 16B in DU-145, PC-3 and LNCaP	IFI 16	IFN	Overexpression inhibits colony formation Senescent morphology[a] SA β-gal assay	(Xin et al., 2003)
Human primary fibroblast cell lines: WS1, WI38, BJ Human mammary epithelial cell lines: 48R and 184	cDNA microarrays of 31,000 genes were used to compared senescent, quiescent and early passage proliferating cells	Select genes upregulated during HMEC M1 senescence *CITED2* *GUK1* *HTATIP2*	Apoptosis Cell cycle IFN IGF Transport		(Zhang et al., 2003)

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
		IGFBP2 *IGFBPrP1* *ISG15* *IGSF3* *RRAS* *STAT1* *TFAP2A* *TNFAIP3* Select genes upregulated during fibroblast senescence *CITED2* *GUK1* *IGFBPrP1* *PEA15* *RRAS* *S100A11* *SERPINB2*	Transcription		
Human diploid fibroblast cell lines WI-38 and BJ	Overexpression of IFI 16 Knockdown of IFI 16 with si-RNA	IFI 16	IFN	Overexpression inhibits colony formation Knockdown extends lifespan; SA β-gal assay	(Xin et al., 2004)
Human dermal fibroblasts (HDF), young compared to old/senescent	Genetrack® Human cDNA 17K microarray	43 upregulated in old HDF including: *Cyclin D1* *IGFBP3* *IGFBP5* *10 IFN genes* *8 inflammation genes* 42 downreguated in old HDF	Cell adhesion Cell cycle Cytoskeleton Cell adhesion Cell proliferation Inflammatory genes Metabolism		(Yoon et al., 2004)
Precrisis, spontaneously immortalized and 5-aza-dC treated immortalized LFS cell lines: MDAH041, MDAH087-N, MDAH087-1, MDAH087-10	Affymetrix HGU95Av2 oligonucleotide microarray Spontaneously immortalized MDAH041 LFS fibroblasts were compared to precrisis LFS fibroblasts and to 5-aza-dC treated immortalized LFS cells	14 epigenetically regulated genes in common to all four LFS cells lines: *ALDH1A3* *CLTB* *CREG* *CYP1B1* *FLJ14675* *HPS5* *HSPA2* *HTATIP2* *IGFBPrP1* *KIAA1750* *MAP1LC3B* *OPTN* *SERPINB2* *TNFAIP2*	IFN Cell cycle Cytoskeleton		(Fridman et al., 2006)

Model System	*Method*	*Gene(s)*	*Pathway(s)*	*Functional Assay*	*Study*
Mouse embryonic fibroblasts and primary human BJ fibroblasts	Suppression of PAI-1 by RNAi Overexpression of PAI-1	*PAI-1*	ECM remodeling Blood coagulation Fibrinolysis Regulation of angiogenesis	Suppression by RNAi results in escape from replicative senescence; assessed by SA β-gal assay, colony formation assay, population doubling Overexpression results in induction of replicative senescence; assessed by SA β-gal assay, colony formation assay	(Kortlever et al., 2006)
Human umbilical vein endothelial cells (HUVEC)	Overexpression of IGFPB5 in HUVEC Exogenous treatment of HUVEC with IGFBP5 Knockdown of IGFBP5	*IGFBP5*	IGF	Overexpression or exogenous treatment of HUVEC cells with IGFBP5 results in induction of replicative senescence; assessed by SA β-gal assay, morphology[a], MTT cell proliferation assay and flow cytometry; increase in p53, $p16^{INK4a}$ and $p21^{CIP1/WAF1}$ protein expression, and decreased pRB phosphorylation Knockdown of IGFBP5 in old senescent HUVEC cells results in a reduction of the senescence phenotype; assessed by SA β-gal assay, morphology[a] and MTT cell proliferation assay; reduction in p53 and $p21^{CIP1/WAF1}$ protein expression, and increased pRB phosphorylation	(Seok Kim et al., 2007)
Primary breast tumor cultures pre- and post-hTERT transduction, and spontaneously immortalized breast cell lines	42,000 feature cDNA microarrays	In hTERT transduced (tumors there were 427 genes upregulated and 170 genes downregulated	Cell cycle Cytoskeleton Oxidative stress pathway		(Dairkee et al., 2007)
Precrisis, spontaneously immortalized and 5-aza-dC treated immortalized LFS cell lines: MDAH041, MDAH087-N, MDAH087-1, MDAH087-10	MDAH041 and MDAH087-1 were transfected with *IGFBP3* and *IGFBPrP1*	*IGFBP3* *IGFBPrP1*	Cell cycle IGF IFN	Inhibits cell growth and colony formation	(Fridman et al., 2007)
Pre-stasis (finite life span), post-statsis (p16 silenced) and immortalized human mammary epithelial cells	Affymetrix U133A/B oligonucleotide microarray		Angiogenesis ECM Cell-cell interactions Actin cytoskeleton Cell cycle		(Li et al., 2007)
Precrisis, spontaneously immortalized and 5-aza-dC treated immortalized LFS cell lines: MDAH041, MDAH087-N, MDAH087-1, MDAH087-10	MDAH041 and MDAH087-1 were transfected with *IRF5* and *IRF7*	*IRF5* *IRF7*	IFN	SA β-gal assay Cell proliferation and life span assays show expression inhibits cell growth	(Li et al., 2008)

Abbreviations: IFN, interferon; IGF, insulin growth factor; MEF, mouse embryonic fibroblast; ND, Not determined
[a]Senescent morphology: enlarged cells with a flat morpholog

Supplemental Table 2. Senescence and immortalization related genes

Gene	*GeneID*[a]	*Chromosome*[b]	*Expression*		*Functional Studies*		*Association with one of the six key senescence/ immortalization pathways*[c]	*References*
			Senescent cells	*Immortalized cells*	*Suppression of gene*	*Ectopic overexpression of the gene*		
AhR	196	7p15		↓			Cell cycle	(Schwarze et al., 2002)
ALDH1	216	9q21.13	↓					(Linskens et al., 1995)
ALDH1A3	220	15q26.3	↑	↓			Regulated by p53 IFN Oxidoreductase activity	(Fridman et al., 2006)
Bmi-1	648	10p11.23	↓			Immortalization	Cell cycle	(Itahana et al., 2003)
BRAK	9547	5q31	↑	↓		Suppresses tumor growth	Immune response; chemokine	(Ozawa et al., 2006; Schwarze et al., 2002)
CD44	960	11p13	↑				Cell adhesion	(Linskens et al., 1995)
CDC25B	994	20p13	↓	↑			Cell cycle	(Fridman et al., 2006; Li et al., 2007)
CITED2	10370	6q23.3	↑				Cell cycle	(Zhang et al., 2003)
CKS-1	137529	8q21.13	↓				Cell cycle	(Untergasser et al., 2002)
CLTB	1212	5q35	↑	↓				(Fridman et al., 2006)
COL1α1	1277	17q21.33	↑↓[d]				Focal adhesion	(Kang et al., 2003; Linskens et al., 1995; Murano et al., 1991)
COL1α2	1278	7q22.1	↑				Focal adhesion	(Murano et al., 1991)
COL3α1	1281	2q31	↓				Focal adhesion	(Linskens et al., 1995)
CREG	8804	1q24	↑	↓		Inhibits growth	Cell cycle	(Di Bacco & Gill, 2003; Fridman et al., 2006)
Cyclin B1	891	5q12	↓				Cell cycle	(Untergasser et al., 2002)
Cyclin D1	595	11q13	↑				Cell cycle	(Chang et al., 2002; Untergasser et al., 2002; Yoon et al., 2004)
CYP1B1	1545	2p21	↑	↓				(Fridman et al., 2006; Kang et al., 2003; Kulaeva et al., 2003)
DOC1	11259	3q21.1	↑	↓			Cytoskeleton	(Kulaeva et al., 2003; Schwarze et al., 2002; Tandle et al., 2005; Zhang et al., 2003)
E2F4	1874	16q21-16q22	↓				Cell cycle	(Untergasser et al., 2002)
EF-1α	10767	6q23-6q24	↑					(Lecka-Czernik et al., 1996)
EGR1	1958	5q31.1	↓				Binds p53	(Untergasser et al., 2002)
EIF-2β	8894	20pter-20q12	↑					(Lecka-Czernik et al., 1996)
Fibronectin	2335	2q34	↑				Cytoskeleton	(Kang et al., 2003; Lecka-Czernik et al., 1996; Murano et al., 1991; Schwarze et al.,

Gene	*GeneID*[a]	*Chromosome*[b]	*Expression*		*Functional Studies*		*Association with one of the six key senescence/ immortalization pathways*[c]	*References*
			Senescent cells	*Immortalized cells*	*Suppression of gene*	*Ectopic overexpression of the gene*		
								2002; Shelton et al., 1999; Suzuki et al., 2001; Untergasser et al., 2002; Zhang et al., 2003)
FLJ14675	84909	9q22	↑	↓				(Fridman et al., 2006)
Gelsolin	2934	9q33	↑				Cytoskeleton	(Fridman et al., 2006; Untergasser et al., 2002)
GUK1	2987	1q32-1q41	↑					(Zhang et al., 2003)
HEREGULIN	3084	8p12	↑				MAP kinase	(Linskens et al., 1995)
HIC5	7041	16p11.2	↑	↓	Delays senescence	Senescence	Cell adhesion	(Shibanuma et al., 1997)
HPS5	11234	11p14	↑	↓			Cytoskeleton	(Fridman et al., 2006)
HSPA2	3306	14q24.1	↑	↓				(Fridman et al., 2006)
HTATIP2	10553	11p15.1	↑	↓	Immortalization		Cell cycle Oxidoreductase activity	(Fridman et al., 2006; Zhang et al., 2003)
HTF (F3)	2152	1p22-p21	↑					(Linskens et al., 1995)
ID1	3397	20q11	↓		Senescence	Immortalization		(Alani et al., 1999; Alani et al., 2001; Untergasser et al., 2002)
IFI 16	3428	1q22	↑	↓	Extends life span	Senescence	Interacts with p53 and pRB IFN	(Xin et al., 2003; Xin et al., 2004)
IFN-γ	3458	12q14	↑				IFN	(Linskens et al., 1995)
IGFBP1	3484	7p13-7p12	↑				IGF	(Fridman et al., 2006; Fridman et al., 2007)
IGFBP2	3485	2q33-2q34	↑	↓			IGF	(Fridman et al., 2006; Fridman et al., 2007; Schwarze et al., 2002; Shelton et al., 1999; Zhang et al., 2003)
IGFBP3	3486	7p13-7p12	↑	↓		Suppresses growth and inhibits colony formation	IGF IFN	(Fridman et al., 2006; Fridman et al., 2007; Goldstein et al., 1991; Kang et al., 2003; Li et al., 2007; Murano et al., 1991; Schwarze et al., 2002; Suzuki et al., 2001; Yoon et al., 2004)
IGFBP4	3487	7q12-7q21.1	↑	↓			IGF IFN	(Fridman et al., 2006; Fridman et al., 2007; Kang et al., 2003; Kulaeva et al., 2003; Suzuki et al., 2001)
IGFBP5	3488	2q33-2q36	↑	↓	Partial reversal senescence phenotype	Senescence	IGF	(Fridman et al., 2006; Fridman et al., 2007; Li et al., 2007; Linskens et al., 1995; Schwarze et al., 2002; Seok Kim et al., 2007; Shelton et al., 1999; Yoon et al., 2004)
IGFBP6	3489	12q13	↑	↓			IGF	(Chang et al., 2002; Fridman et al., 2006; Fridman et al., 2007; Kulaeva et al., 2003)
IGFBPrP1	3490	4q12	↑	↓		Senescence	Cell cycle	(Fridman et al., 2006; Fridman et al., 2007;

Gene	*GeneID*[a]	*Chromosome*[b]	*Expression*		*Functional Studies*		*Association with one of the six key senescence/ immortalization pathways*[c]	*References*
			Senescent cells	*Immortalized cells*	*Suppression of gene*	*Ectopic overexpression of the gene*		
							IGF	Lopez-Bermejo et al., 2000; Swisshelm et al., 1995; Wilson et al., 2002; Zhang et al., 2003)
IGFBPrP2 (CTGF; IGFBP8)	1490	6q23.1	↑	↓			Cell adhesion IGF	(Fridman et al., 2006; Fridman et al., 2007; Kang et al., 2003; Lopez-Bermejo et al., 2000; Schwarze et al., 2002)
IGFBPrP5 (HTRA1; PRSS11)	5654	10q26.3		↓			IGF	(Fridman et al., 2006; Fridman et al., 2007)
IGFBPrP6 (ESM1)	11082	5q11.2	↑	↑↓[d]			Regulated by cytokines IGF	(Fridman et al., 2006; Fridman et al., 2007)
IGFBPrP8 (WISP1)	8840	8q24.1-8q24.3	↓	↑			Cell adhesion IGF	(Fridman et al., 2006; Fridman et al., 2007; Kulaeva et al., 2003)
IGF1R	3480	15q26.3		↑			Cell cycle IGF	(Fridman et al., 2006; Fridman et al., 2007)
IGSF3	3321	1p13	↑				Immune system	(Zhang et al., 2003)
IRF5	3663	7q32	↑	↓		Senescence	IFN	(Li et al., 2008)
IRF7	3665	11p15.5	↑	↓		Senescence	IFN	(Kulaeva et al., 2003; Li et al., 2008; Liang et al., 2002)
ISG15	9636	1p36.33	↑				IFN	(Zhang et al., 2003)
KIAA1750	85453	8q22.1	↑	↓				(Fridman et al., 2006)
LAMININA	284217	18p11.31	↓				Cell adhesion	(Linskens et al., 1995)
LDB2	9079	4p16	↓	↑				(Fridman et al., 2006)
MAP1LC3B	81631	16q24.2	↑	↓			Cytoskeleton	(Fridman et al., 2006)
MDM2	4193	12q14.3-12q15	↑				Cell cycle	(Schwarze et al., 2002)
MKK3	5606	17q11.2	↑	↓		Senescence	MAP kinase	(Fridman et al., 2006; Wang et al., 2002)
MKK6	5608	17q24.3				Senescence	Cell cycle MAP kinase	(Haq et al., 2002; Wang et al., 2002)
MMP1	4312	11q22.3	↑					(Kang et al., 2003)
MORF4	10934	4q33-4q34.1				Senescence		(Bertram et al., 1999; Berube et al., 1998)
c-MYC	4609	8q24.21				Immortalization	Cell cycle	(Bringold & Serrano, 2000; Gil et al., 2005)
NDN	4692	15q11.2-15q12	↑	↓			Cell cycle Cytoskeleton	(Kulaeva et al., 2003)
nm23-H2	4831	17q21.3	↑				Cell cycle Cell adhesion	(Lecka-Czernik et al., 1996)
OPTN	10133	10p13	↑	↓			IFN	(Fridman et al., 2006)

Gene	*GeneID*[a]	*Chromosome*[b]	*Expression*		*Functional Studies*		*Association with one of the six key senescence/ immortalization pathways*[c]	*References*
			Senescent cells	*Immortalized cells*	*Suppression of gene*	*Ectopic overexpression of the gene*		
Osteonectin	6678	5q31.3-5q32	↑	↓			Cell cycle Cytoskeleton	(Kang et al., 2003; Lecka-Czernik et al., 1996; Murano et al., 1991; Schwarze et al., 2002)
p14^{ARF}	1029	9p21				Senescence	Cell cycle	(Sekaric et al., 2007; Shamanin & Androphy, 2004)
p15^{INK4b}	1030	9p21	↑			Senescence	Cell cycle	(Kang et al., 2003; Roninson, 2003)
p16^{INK4a}	1029	9p21	↑	↓		Senescence	Cell cycle	(Kang et al., 2003; Schwarze et al., 2002; Tsutsui et al., 2002; Vogt et al., 1998)
p19^{INK4d}	1032	19p13	↑				Cell cycle	(Kang et al., 2003)
p21$^{CIP1/WAF1}$	1026	6p21.2	↑	↓		Senescence	Cell cycle	(Chang et al., 2002; Schwarze et al., 2002; Suzuki et al., 2001; Vogt et al., 1998; Wells et al., 2003)
p33ING1	3621	13q34	↑		Extends life span	Senescence	Cell cycle	(Berube et al., 1998; Garkavtsev & Riabowol, 1997; Goeman et al., 2005)
p38HOG	1432	6p21.3-6p21.2				Senescence	Cell cycle MAP kinase Oxidative	(Haq et al., 2002; Wang et al., 2002)
p53	7157	17p13.1	↑	↓	Extends life span	Senescence	Cell cycle	(Bischoff et al., 1990; Bischoff et al., 1991; Fridman et al., 2006; Harvey et al., 1993; Rogan et al., 1995; Roninson, 2003; Serrano et al., 1997; Sugrue et al., 1997; Tsutsui et al., 1997)
p57	1028	11p15.5	↑			Senescence	Cell cycle	(Kang et al., 2003; Roninson, 2003; Wells et al., 2003)
p130	5934	16q12.2	↑				Cell cycle	(Wells et al., 2003)
PAI-1	5054	7q21.3-7q22	↑	↓	Senescence	Immortalization	Cell cycle Cytoskeleton	(Kortlever et al., 2006; Lecka-Czernik et al., 1996; Li et al., 2007; Murano et al., 1991; Shelton et al., 1999; Suzuki et al., 2001; Untergasser et al., 2002)
PEA15	8682	1q21.1	↑				Cytoskeleton MAP kinase	(Zhang et al., 2003)
pRB	5925	13q14.2		↓	Immortalization	Senescence	Cell cycle	(Berube et al., 1998; Roninson, 2003)
RAB13	5872	1q21.2	↑				Cell adhesion	(Wells et al., 2003)
RAB2L	5863	6p21.3	↑					(Wells et al., 2003)
RAB31	11031	18p11.3	↑					(Wells et al., 2003)
RAB5B	5869	12q13	↑					(Wells et al., 2003)
RABGGTA	5875	14q11.2	↑					(Wells et al., 2003)
RAC1	5879	7p22	↑				Cell adhesion Cell cycle	(Untergasser et al., 2002)

Gene	*GeneID*[a]	*Chromosome*[b]	*Expression*		*Functional Studies*		*Association with one of the six key senescence/ immortalization pathways*[c]	*References*
			Senescent cells	*Immortalized cells*	*Suppression of gene*	*Ectopic overexpression of the gene*		
							Cytoskeleton Inflammatory response	
RhoB	388	2p24	↑				Cell cycle Cell adhesion	(Schwarze et al., 2002)
RAS (H-ras V12)	3265	11p15.5				Senescence ($p16^{INKa}$ and p53 dependent)	Cytoskeleton MAP kinase	(Serrano et al., 1997)
RRAS	6237	19q13.3-qter	↑				Cytoskeleton MAP kinase	(Zhang et al., 2003)
S100A11	6282	1q21	↑	↓			Cell cycle Cytoskeleton	(Sakaguchi et al., 2000; Sakaguchi et al., 2001; Zhang et al., 2003)
SERPINB2	5055	18q21.3	↑	↓			Interacts with pRB IFN	(Fridman et al., 2006; Liang et al., 2002; Linskens et al., 1995; Zhang et al., 2003)
SMURF2	64750	17q22-17q23	↑			Senescence	Cell cycle	(Zhang & Cohen, 2004)
SOD	6647	21q22.11	↑				Oxidoreductase activity	(Linskens et al., 1995)
Sphingomyelinase	6609	11p15.4-11p15.1	↑					(Lecka-Czernik et al., 1996)
STAT1	6772	2q32.2	↑	↓		Insufficient to growth arrest or senesce cells	IFN	(Kulaeva et al., 2003; Liang et al., 2002; Tang et al., 2006; Zhang et al., 2003)
hTERT	7015	5p15.33		↑		Extends life span		(Bodnar et al., 1998; Kulaeva et al., 2003)
TES	26136	7q31.2	↑	↓			Cytoskeleton	(Fridman et al., 2006; Kulaeva et al., 2003)
TFAP2A	7020	6p24	↑					(Liang et al., 2002; Zhang et al., 2003)
Thrombospondin	7057	15q15	↑				Cell adhesion	(Lecka-Czernik et al., 1996; Murano et al., 1991)
TNFAIP2	7127	14q32	↑	↓				(Fridman et al., 2006)
TNFAIP3	7128	6q23	↑				Immune	(Liang et al., 2002; Zhang et al., 2003)
Vimentin	7431	10p13	↑	↓			Cytoskeleton	(Kaneko et al., 1995; Satoh et al., 1994; Untergasser et al., 2002)
αB-crystallin	1410	11q22.3-11q23.1	↑					(Murano et al., 1991)
80K-L	4082	6q22.2	↓				Cytoskeleton	(Linskens et al., 1995)

Abbreviations: IFN, interferon; IGF, insulin growth factor
[a]GeneID: http://www.ncbi.nlm.nih.gov/sites/entrez
[b]Chromosome location obtained from NCBI GeneID record
[c]Based on information from the literature and from NCBI (http://www.ncbi.nlm.nih.gov/sites/entrez)
[d]Expression is cell line dependent

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