Supplementary Table 2. Link of experimentally observed targets for differentially expressed miRNAs to canonical pathways and cellular functions.

Targets	Association	Reference
link of miRNAs to normal aging – miR-34a-5p		
Axin2, Wnt family members (WNT1, WNT3), β-catenin (CTNNB1)	Wnt signaling pathway: cell renewal and tissue homeostasis	[1, 2]
Jagged1 (JAG1), Notch receptors NOTCH1, NOTCH2), delta-like ligands (DLL1)	Notch signaling pathway: cell differentiation and senescence	[3]
p53, sirtuin 1 (SIRT1)	modulators of the aging processes: regulate DNA damage responses, apoptosis, and survival	[4]
mitogen-activated protein kinase kinase 1 (MEK1), SMAD3, and TGF beta receptor 1 (TGFBR1)	aging-associated pathways: MAPK/ERK and TGF-β pathways: cell proliferation and repair	[5]
MYC, MYCN	Proto-oncogenes: cellular metabolism and growth	[6]
Histone deacetylase 1 (HDAC1) and chromodomain helicase DNA binding protein 8 (CHD8)	epigenetic regulators: gene expression: chromatin state, DNA methylation, histone modification, chromatin remodeling	[7, 8]
link of miRNAs to normal aging – miR-92a-3p		
cyclin E2, cyclin-dependent kinase inhibitors 1A and 1C, F-box and WD repeat domain-containing 7 (FBXW7)	cell cycle regulation, maintenance of cellular homeostasis: stem cell aging	[9, 10]
BCL2-like 11 (BCL2L11)	apoptosis, cell proliferation	[11]
phosphatase and tensin homolog (PTEN)	modulator of survival	[12]
Polycomb group proteins (PCGF1, ZEB2)	chromatin remodeling	[13, 14]
Integrins (ITGA5, ITGB3) and bone morphogenetic protein receptor type 2 (BMPR2)	inflammation and age-related fibrosis	[15–17]
oxysterol binding proteins (OSBPL2, OSBPL8)	lipid metabolism; oxidative stress	[18]
mitogen-activated protein kinase kinase 4 (MAP2K4)	MAPK pathway: stress response and senescence	[19]
link of miRNAs to HGPS cellular aging – miR-126-3p; miR-126-5p		
forkhead box O3 (FOXO3)	key longevity factor: oxidative stress responses, autophagy, apoptosis: helping protect cells from age-related damage	[20, 21]
solute carrier family 45 member 3 (SLC45A3)	immune cell infiltration, cellular homeostasis	[22]
link of miRNAs to HGPS cellular aging – miR-200a/b		
BRCA1-associated protein 1 (BAP1)	chromatin remodeling, DNA repair, and genomic stability	[23, 24]
ERBB2 interacting protein (ERBIN), engulfment and cell motility 2 (ELMO2)	cell growth, polarity, motility, and cytoskeletal organization, tissue regeneration	[25–28]
GEM nuclear organelle-associated protein 2 (GEMIN2)	nuclear structure	[29, 30]
zinc finger E-box binding homeobox 1 and 2 (ZEB1, ZEB2)	stem cell differentiation, epithelial-to-mesenchymal transition (EMT): tissue repair and fibrosis	[31, 32]
Kelch like family member 20 (KLHL20)	protein homeostasis: counteracting age-related cellular damage	[33, 34]
link of miRNAs to early changes in HGPS		
B-cell lymphoma 2 (BCL2), programmed cell death 4 (PDCD4)	apoptosis modulators: cell death and tissue degeneration	[35–37]
brain-derived neurotrophic factor (BDNF), epidermal growth factor receptor (EGFR), insulin-like growth factor 1 (IGF-1), growth factor receptor bound protein 2 (GRB2)	cellular growth and repair: tissue regeneration and neurodegeneration with age	[38–42]

H3.3 histone A	chromatin structure and gene expression: cellular senescence	[43–46]
Polo-like kinase 1 (PLK1), WEE1 G2 checkpoint kinase (WEE1)	cell cycle, maintaining genomic stability	[47, 48]
link of miRNAs to premature aging		
BCL2, PDCD4	apoptosis regulators: cell death and tissue degeneration	[35–37, 49]
Cyclin D1 (CCND1)	cell cycle, senescence	[50, 51]
MAP2K4	RAS/MAPK signaling pathway: cell proliferation and survival, senescence	[52]
NOTCH2	cell adhesion, differentiation, and tissue homeostasis	[53, 54]

Target analysis of genome-wide miRNA sequencing of HGPS and control fibroblast cultures of a young passage with relative senescence < 5 % and an old passage of senescence between 15 and 20 %; control cell strains: GM01651c, GM01652c, GM03349c; HGPS cell strains: HGADFN003, HGADFN127, HGADFN178.

Supplementary Table 3. Passage numbers of young and old cell cultures for each primary fibroblast cell strain.

Cell Strain	Young culture senescence < 5%	Old culture senescence 15-20%
GM01651	Passage 14-17	Passage 23-25
GM01652	Passage 15-18	Passage 24-26
GM03349	Passage 16-18	Passage 22-26
GM05757	Passage 15-17	-
GM05565	Passage 14-18	-
HGADFN003	Passage 12-15	Passage 21-23
HGADFN127	Passage 11-14	Passage 18-19
HGADFN178	Passage 11-13	Passage 15-17
HGADFN164	Passage 10-14	-

Supplementary Table 4. List of primer pairs with forward (F), reverse (R), and reverse transcription (RT) primer sequences.

Target gene	Primer sequence (5’ to 3’)
mmu-miR-145a-5p	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAGGGATTC F: AACAAGGTCCAGTTTTCCCAG R: GTCGTATCCAGTGCAGGGT
mmu-miR-27b-3p	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAGGGATTC F: AACAAGGTCCAGTTTTCCCAG R: GTCGTATCCAGTGCAGGGT
mmu_C/EBPα	F: AGGTGCTGGAGTTGACCAGT R: CAGCCTAGAGATCCAGCGAC
mmu_PPARγ	F: CAAGAATACCAAAGTGCGATCAA R: GAGCTGGGTCTTTTCAGAATAATAAG
mmu_FABP4	F: AAGACAGCTCCTCCTCGAAGGTT R: TGACCAAATCCCCATTTACGC
mmu_U6	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAAAATA F: CTCGCTTCGGCAGCACA R: AACGCTTCACGAATTTGCGT
mmu_GAPDH	F: TTGTTGCCATCAACGACCCC R: GCCGTTGAATTTGCCGTGAG
hsa-miR-145-5p	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAGGGATTC F: AACAAGGTCCAGTTTTCCCAG R: GTCGTATCCAGTGCAGGGT
hsa-miR-27b-3p	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACGCGGAACT F: AACACGCTTCACGTGGCTA R: GTCGTATCCAGTGCAGGGT
hsa_C/EBPα	F: AGGAGGATGAAGCCAAGCAGCT R: AGTGCGCGATCTGGAACTGCAG
hsa_PPARγ	F: GGCTTCACATTCAGCAAACCTGG R: AGCCTGCGAAAGCCTTTTGGTG
hsa_FABP4	F: ACCAGAGGATGATAAACTGGTGG R: GCGAACTTCAGTCCAGGTGAAC
hsa_PHB	F: AAGCGGTGGAAGCCAAACAGGT R: GCCAGTGAGTTGGCAATCAGCT
hsa_LPL	F: TGGAGGTACTTTTCAGCCAGGAT R: TCGTGGGAGCACTTCACTAGCT
hsa_IRS1	F: GGAGTACATGAAGATGGACCTGG R: CTGTTCGCATGTCAGCATAGC
hsa_KLF4	F: CATCTCAAGGCACACCTGCGAA R: TCGGTCGCATTTTTGGCACTGG
hsa_KLF5	F: GGAGAAACGACGCATCCACTAC R: GAACCTCCAGTCGCAGCCTTC
hsa_U6	RT: GTCGTATCCAGTGCAGGGTCCGAGGTATTCGCACTGGATACGACAAAATA F: CTCGCTTCGGCAGCACA R: AACGCTTCACGAATTTGCGT
hsa_GAPDH	F: GTCTCCTCTGACTTCAACAGCG R: ACCACCCTGTTGCTGTAGCCAA

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