Supplementary Information

In Vivo Base Editing Rescues Hutchinson-Gilford Progeria Syndrome in Mice

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Supplementary Note 1. Description of censored mice in the longevity study.

One female mouse injected with ABE-AAV9 at P14 was found dead following an unknown abdominal trauma at 186 days of age.

Following a urethra prolapse and subsequent infection, one male mouse injected with ABE-AAV9 at P3 was euthanized at 279 days of age.

One male mouse injected with ABE-AAV9 at P14 was euthanized at 303 days of age following an obstructive uropathy, a previously reported occurrence in C57BL/6 mice[64].

Supplementary Note 2. Lentivirus and adeno-associated virus plasmid sequences

Lentiviral ABEmax-VRQR + LMNA sgRNA vector sequence

CMV promoter
Lenti LTRs
psi
gag
RRE
CPPT
U6 promoter
LMNA sgRNA
SpCas9 scaffold
EFS promoter
ABEmax **VRQR**
P2A
Puromycin
WPRE
BGH poly-A
F1 origin
SV40 rep
Bleomycin
SV40 poly-A
pUC origin
Amp Resistance

GTCGACGGATCGGGAGATCTCCCGATCCCCTATGGTGCACTCTCAGTACAATCTGCTCT
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AAV Constructs

AAV ITR
Cbh promoter
Bipartite NLS
rAPOBEC1 (CBEmax)
tadA (ABEmax)
Linkers
Cas9 (N- or C-terminal specified in construct title)
Npu N-terminal fragment
Npu C-terminal fragment
UGI
W3
bGH
U6-sgRNA
sgRNA spacer
HGPS protospacer

ABEmax v5 AAV N-terminal (Same as Addgene plasmid #137178)

CTGCGCGCTCGCTCGCTCACTGAGGCCGCCCGGGCAAAGCCCGGGCGTCGGGCGACC
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ABEmax v5 AAV C-terminal, LMNA c.1824 C→T protospacer

This construct has BsmBI sites flanking an RFP dropout cassette to facilitate selection. Bacteria transformed with uncut parent vector will be RFP-positive.

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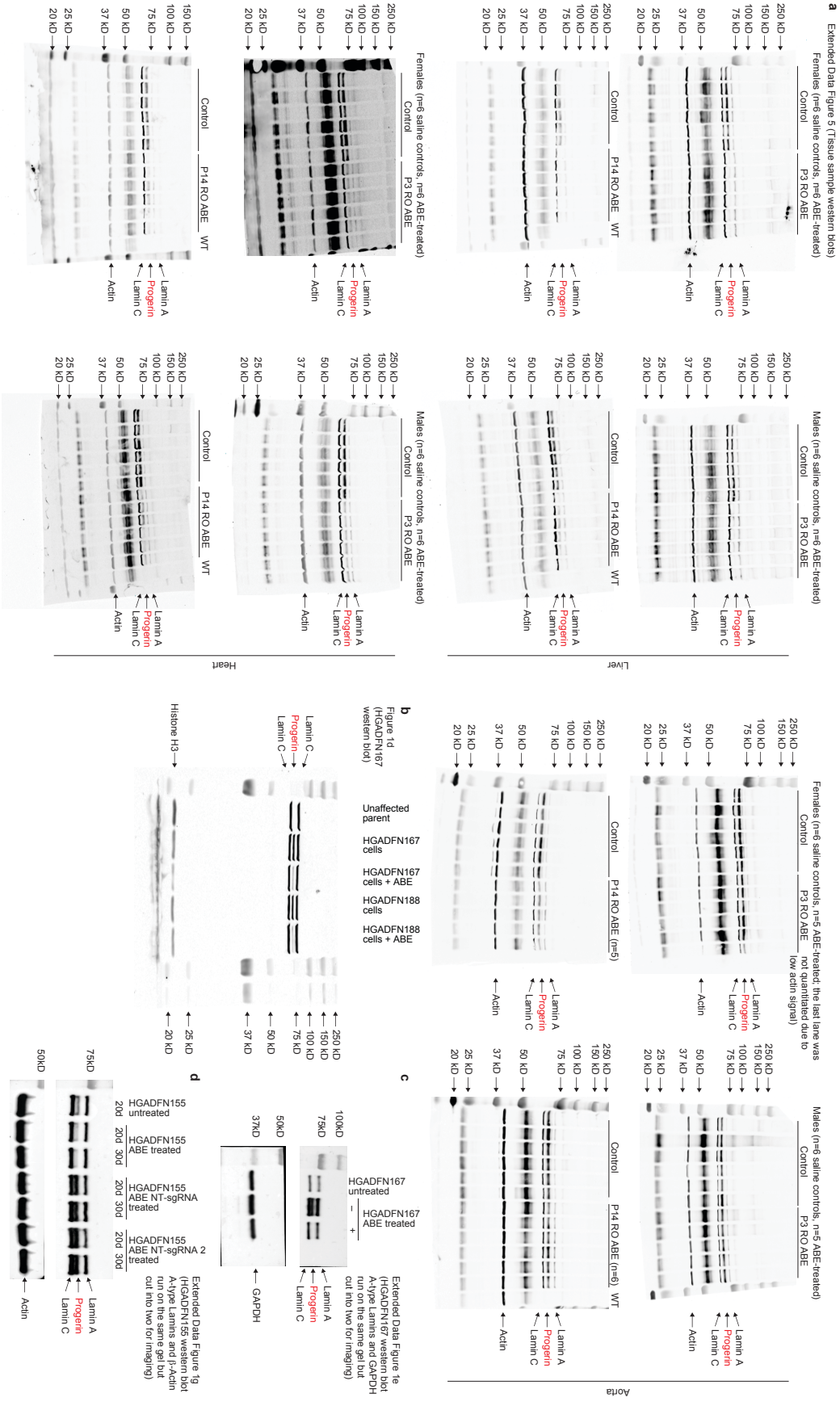
Supplementary Note 3. Scripts used in this study.

Scripts used in this study can be downloaded from:
https://github.com/CwilsonBroad/Koblan_2020_In-Vivo-Adenine-Base-Editing-Corrects-Hutchinson-Gilford-Progeria-Syndrome.

Supplementary Figure 1. Complete gel images of western blots.



Supplementary Table 1. Information on animals in the longevity study. P3-injected mice showed an increase in keratitis of the eye that may have arisen from retro-orbital injections at an early age, possibly contributing to the shorter median lifespan of P3-injected saline-treated control mice relative to P14-injected saline control mice.

Inj age	Injected material	Injection route	Sex	ID	Genotype	DOB	Inj date	DOD	Age (d)	Excluded?	Cause of death
P3	Dual ABE AAV9	Retro-orbital sinus	F	F109166	Homozygous	1/18/19	1/21/19	1/3/20	351	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	F	F209167	Homozygous	1/18/19	1/21/19	1/2/20	350	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	F	F2+409170	Homozygous	1/18/19	1/21/19	1/3/20	351	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	F	F109175	Homozygous	1/18/19	1/21/19	12/5/19	322	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	F	F209176	Homozygous	1/18/19	1/21/19	12/25/19	342	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	F	F2+409180	Homozygous	1/18/19	1/21/19	12/25/19	342	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F309629	Homozygous	6/2/19	6/4/19	12/8/19	190	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F209636	Homozygous	6/2/19	6/4/19	12/8/19	190	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F3+609637	Homozygous	6/2/19	6/4/19	12/8/19	190	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F109650	Homozygous	6/9/19	6/12/19	12/8/19	183	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F3+409652	Homozygous	6/9/19	6/12/19	12/8/19	183	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	F	F3+509659	Homozygous	6/14/19	6/17/19	12/8/19	178	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M2+409178	Homozygous	1/18/19	1/21/19	12/31/19	348	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M209211	Homozygous	1/20/19	1/23/19	12/16/19	331	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M3+409212	Homozygous	1/20/19	1/23/19	12/6/19	321	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M109127	Homozygous	1/20/19	1/23/19	12/16/19	331	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M209128	Homozygous	1/20/19	1/23/19	12/18/19	333	N	Endpoint necopsy; likely complications associated with HGPS
P3	Dual ABE AAV9	Retro-orbital sinus	M	M2+409133	Homozygous	1/20/19	1/23/19	10/25/19	279	Y	Emergency necropsy; penile prolapse
P3	Saline	Retro-orbital sinus	M	M209631	Homozygous	6/2/19	6/4/19	1/20/20	233	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	M	M309632	Homozygous	6/2/19	6/4/19	1/20/20	233	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	M	M409461	Homozygous	6/2/19	6/4/19	1/20/20	233	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	M	M5+109642	Homozygous	6/2/19	6/4/19	12/6/19	188	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	M	M3+409649	Homozygous	6/5/19	6/8/19	12/14/19	193	N	Endpoint necopsy; likely complications associated with HGPS
P3	Saline	Retro-orbital sinus	M	M2+409654	Homozygous	6/9/19	6/12/19	12/14/19	193	N	Endpoint necopsy; likely complications associated with HGPS
P14	Dual ABE AAV9	Retro-orbital sinus	F	F3+609503	Homozygous	5/4/19	5/17/19	9/29/20	515	N	Endpoint necropsy; no abnormalities, likely complications associated w/HGPS
P14	Dual ABE AAV9	Retro-orbital sinus	F	F1+609524	Homozygous	5/4/19	5/17/19	9/23/20	509	N	Endpoint necropsy; lower lobe liver tumors
P14	Dual ABE AAV9	Retro-orbital sinus	F	F2+409525	Homozygous	5/4/19	5/17/19	11/6/19	187	Y	Found dead; thoracic trauma
P14	Dual ABE AAV9	Retro-orbital sinus	F	F1+609529	Homozygous	5/5/19	5/17/19			N	(Still alive as of 11/06/2020)
P14	Dual ABE AAV9	Retro-orbital sinus	F	F409532	Homozygous	5/5/19	5/17/19		534	N	Endpoint necopsy; likely complications associated with HGPS
P14	Dual ABE AAV9	Retro-orbital sinus	F	F3+409547	Homozygous	5/4/19	5/17/19	9/25/20	511	N	Endpoint necropsy; no abnormalities, likely complications associated w/HGPS
P14	Saline	Retro-orbital sinus	F	F109481	Homozygous	4/27/19	5/15/19	11/25/19	213	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	F	F209496	Homozygous	4/27/19	5/15/19	11/25/19	213	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	F	F309508	Homozygous	4/27/19	5/15/19	11/25/19	213	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	F	F309537	Homozygous	5/3/19	5/15/19	12/4/19	216	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	F	F409517	Homozygous	5/3/19	5/15/19	12/6/19	218	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	F	F4+309561	Homozygous	5/4/19	5/15/19	12/4/19	215	N	Endpoint necopsy; likely complications associated with HGPS
P14	Dual ABE AAV9	Retro-orbital sinus	M	M109485	Homozygous	4/27/19	5/19/19	9/20/20	513	N	Endpoint necropsy: abdominal lesion; upper- mid- lower- left lobe liver tumors
P14	Dual ABE AAV9	Retro-orbital sinus	M	M1+609504	Homozygous	5/4/19	5/19/19	4/29/20	361	N	Found dead; gastrointestinal necrosis
P14	Dual ABE AAV9	Retro-orbital sinus	M	M209528	Homozygous	5/4/19	5/19/19	3/2/20	322	Y	Endpoint necopsy; obstructive uropathy
P14	Dual ABE AAV9	Retro-orbital sinus	M	M3+409544	Homozygous	5/4/19	5/19/19	8/3/20	458	N	Endpoint necropsy: lower lobe liver tumor
P14	Dual ABE AAV9	Retro-orbital sinus	M	M1+409548	Homozygous	5/4/19	5/19/19	7/24/20	448	N	Endpoint necopsy; mid- and lower lobe liver tumor; enlarged heart
P14	Dual ABE AAV9	Retro-orbital sinus	M	M3+609550	Homozygous	5/4/19	5/19/19	7/14/20	438	N	Endpoint necopsy; proximal and mid-lobe liver tumor
P14	Saline	Retro-orbital sinus	M	M209498	Homozygous	4/27/19	5/19/19	11/28/19	216	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	M	M409500	Homozygous	4/27/19	5/19/19	11/28/19	216	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	M	M109510	Homozygous	4/27/19	5/19/19	11/28/19	216	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	M	M409551	Homozygous	5/4/19	5/19/19	12/18/19	229	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	M	M309512	Homozygous	4/27/19	5/19/19	12/21/19	239	N	Endpoint necopsy; likely complications associated with HGPS
P14	Saline	Retro-orbital sinus	M	M109533	Homozygous	5/5/19	5/19/19	12/21/19	231	N	Endpoint necopsy; likely complications associated with HGPS

Supplementary Table 2. Statistical analysis.

Cell line transcript abundance (Figure 1c)

Quantitation:	Cell line:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
LMNA transcript abundance	HGADFN167	Untreated	10 day ABE-treated	0.0119	Two-tailed	t=4.376 df=4
LMNA transcript abundance	HGADFN167	Untreated	20 day ABE-treated	0.3475	Two-tailed	t=1.063 df=4
Progerin transcript abundance	HGADFN167	Untreated	10 day ABE-treated	< 0.0001	Two-tailed	t=122.8 df=4
Progerin transcript abundance	HGADFN167	Untreated	20 day ABE-treated	< 0.0001	Two-tailed	t=50.74 df=4
LMNC transcript abundance	HGADFN167	Untreated	10 day ABE-treated	0.8121	Two-tailed	t=0.2538 df=4
LMNC transcript abundance	HGADFN167	Untreated	20 day ABE-treated	0.0604	Two-tailed	t=2.595 df=4
LMNA transcript abundance	HGADFN188	Untreated	10 day ABE-treated	0.1035	Two-tailed	t=2.101 df=4
LMNA transcript abundance	HGADFN188	Untreated	20 day ABE-treated	0.0152	Two-tailed	t=4.075 df=4
Progerin transcript abundance	HGADFN188	Untreated	10 day ABE-treated	< 0.0001	Two-tailed	t=16.61 df=4
Progerin transcript abundance	HGADFN188	Untreated	20 day ABE-treated	< 0.0001	Two-tailed	t=18.11 df=4
LMNC transcript abundance	HGADFN188	Untreated	10 day ABE-treated	0.5097	Two-tailed	t=0.7229 df=4
LMNC transcript abundance	HGADFN188	Untreated	20 day ABE-treated	0.0043	Two-tailed	t=5.818 df=4

Abnormal nuclei counts (Figure 1f)

Quantitation:	Cell line:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
Abnormal Nuclei	HGADFN167	Untreated	20 day treated	< 0.0001	Two-tailed	t=17.50 df=4

Cell line A-to-I editing frequencies (Figure 2c)

Quantitation:	Cell line:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
% A-to-I editing	HGADFN167	Untreated	10 day ABE-treated	0.0835	Two-tailed	t=2.293 df=4
% A-to-I editing	HGADFN167	Untreated	20 day ABE-treated	0.1758	Two-tailed	t=1.642 df=4
% A-to-I editing	HGADFN188	Untreated	10 day ABE-treated	0.284	Two-tailed	t=1.236 df=4
% A-to-I editing	HGADFN188	Untreated	20 day ABE-treated	0.9677	Two-tailed	t=0.04312 df=4

P3 6 week ABE-treated versus 6 month ABE-treated DNA editing efficiencies (Figure 3b)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
P3 6wk vs. 6mo DNA editing	Heart	6 week ABE-treated	6 monthABE- treated	0.0051	Two-tailed	t=3.318 df=14
P3 6wk vs. 6mo DNA editing	Quad	6 week ABE-treated	6 monthABE- treated	0.0112	Two-tailed	t=2.918 df=14
P3 6wk vs. 6mo DNA editing	Liver	6 week ABE-treated	6 monthABE- treated	0.2039	Two-tailed	t=1.333 df=14
P3 6wk vs. 6mo DNA editing	Aorta	6 week ABE-treated	6 monthABE- treated	0.0028	Two-tailed	t=3.625 df=14
P3 6wk vs. 6mo DNA editing	Bone	6 week ABE-treated	6 monthABE- treated	0.0003	Two-tailed	t=4.757 df=14

P14 6 week ABE-treated versus 6 month ABE-treated DNA editing efficiencies (Figure 3b)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
P14 6wk vs. 6mo DNA editing	Heart	6 week ABE-treated	6 monthABE- treated	0.0008	Two-tailed	t=4.196 df=15
P14 6wk vs. 6mo DNA editing	Quad	6 week ABE-treated	6 monthABE- treated	0.0048	Two-tailed	t=3.304 df=15
P14 6wk vs. 6mo DNA editing	Liver	6 week ABE-treated	6 monthABE- treated	0.0906	Two-tailed	t=1.808 df=15
P14 6wk vs. 6mo DNA editing	Aorta	6 week ABE-treated	6 monthABE- treated	0.5735	Two-tailed	t=0.5755 df=15
P14 6wk vs. 6mo DNA editing	Bone	6 week ABE-treated	6 monthABE- treated	0.0683	Two-tailed	t=1.965 df=15

P3 6 month ABE-treated versus P14 6 month ABE-treated DNA editing efficiencies (Extended Data Figure 3c)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
P3 vs P14 DNA editing (6mo)	Aorta	P3 6 month ABE-treated	P14 6 month ABE-treated	< 0.0001	Two-tailed	t=4.846 df=22
P3 vs P14 DNA editing (6mo)	Heart	P3 6 month ABE-treated	P14 6 month ABE-treated	0.0382	Two-tailed	t=2.205 df=22
P3 vs P14 DNA editing (6mo)	Kidney	P3 6 month ABE-treated	P14 6 month ABE-treated	0.4461	Two-tailed	t=0.7759 df=22
P3 vs P14 DNA editing (6mo)	Liver	P3 6 month ABE-treated	P14 6 month ABE-treated	0.0059	Two-tailed	t=3.051 df=22
P3 vs P14 DNA editing (6mo)	Lung	P3 6 month ABE-treated	P14 6 month ABE-treated	0.0185	Two-tailed	t=2.544 df=22
P3 vs P14 DNA editing (6mo)	Quad	P3 6 month ABE-treated	P14 6 month ABE-treated	< 0.0001	Two-tailed	t=5.188 df=22
P3 vs P14 DNA editing (6mo)	Skin	P3 6 month ABE-treated	P14 6 month ABE-treated	0.4918	Two-tailed	t=0.6991 df=22
P3 vs P14 DNA editing (6mo)	Spleen	P3 6 month ABE-treated	P14 6 month ABE-treated	0.6707	Two-tailed	t=0.4309 df=22
P3 vs P14 DNA editing (6mo)	Bone	P3 6 month ABE-treated	P14 6 month ABE-treated	0.0113	Two-tailed	t=2.763 df=22
P3 vs P14 DNA editing (6mo)	Visc. fat	P3 6 month ABE-treated	P14 6 month ABE-treated	0.0505	Two-tailed	t=2.069 df=22
P3 vs P14 DNA editing (6mo)	WAT	P3 6 month ABE-treated	P14 6 month ABE-treated	0.476	Two-tailed	t=0.7252 df=22

P3 6 month saline-treated versus P3 6 month ABE-treated ddPCR transcript abundance (Figure 3c, Extended Data Figure 4)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
Progerin transcript abundance	Liver	6mo P3 saline-treated	6mo P3 ABE-treated	< 0.0001	Two-tailed	t=5.509 df=22
Progerin transcript abundance	Heart	6mo P3 saline-treated	6mo P3 ABE-treated	0.3146	Two-tailed	t=1.029 df=22
Progerin transcript abundance	Aorta	6mo P3 saline-treated	6mo P3 ABE-treated	0.1811	Two-tailed	t=1.381 df=22
Progerin transcript abundance	Quad	6mo P3 saline-treated	6mo P3 ABE-treated	0.1091	Two-tailed	t=1.670 df=22
Progerin transcript abundance	Bone	6mo P3 saline-treated	6mo P3 ABE-treated	0.2405	Two-tailed	t=1.206 df=22
Progerin transcript abundance	Skin	6mo P3 saline-treated	6mo P3 ABE-treated	0.4948	Two-tailed	t=0.6942 df=22
Progerin transcript abundance	Visc. Fat	6mo P3 saline-treated	6mo P3 ABE-treated	0.5597	Two-tailed	t=0.5923 df=22
Progerin transcript abundance	WAT	6mo P3 saline-treated	6mo P3 ABE-treated	< 0.0001	Two-tailed	t=5.587 df=22
Progerin transcript abundance	lung	6mo P3 saline-treated	6mo P3 ABE-treated	0.7648	Two-tailed	t=0.3029 df=22
Progerin transcript abundance	Kidney	6mo P3 saline-treated	6mo P3 ABE-treated	< 0.0001	Two-tailed	t=4.837 df=22
Progerin transcript abundance	Spleen	6mo P3 saline-treated	6mo P3 ABE-treated	0.597	Two-tailed	t=0.5366 df=22
LMNA transcript abundance	Liver	6mo P3 saline-treated	6mo P3 ABE-treated	0.0019	Two-tailed	t=3.523 df=22
LMNA transcript abundance	Heart	6mo P3 saline-treated	6mo P3 ABE-treated	0.0018	Two-tailed	t=3.549 df=22
LMNA transcript abundance	Aorta	6mo P3 saline-treated	6mo P3 ABE-treated	0.0431	Two-tailed	t=2.147 df=22
LMNA transcript abundance	Quad	6mo P3 saline-treated	6mo P3 ABE-treated	0.6065	Two-tailed	t=0.5226 df=22
LMNA transcript abundance	Bone	6mo P3 saline-treated	6mo P3 ABE-treated	0.3633	Two-tailed	t=0.9283 df=22
LMNA transcript abundance	Skin	6mo P3 saline-treated	6mo P3 ABE-treated	0.05	Two-tailed	t=2.074 df=22
LMNA transcript abundance	Visc. Fat	6mo P3 saline-treated	6mo P3 ABE-treated	0.1342	Two-tailed	t=1.555 df=22
LMNA transcript abundance	WAT	6mo P3 saline-treated	6mo P3 ABE-treated	0.0036	Two-tailed	t=3.262 df=22
LMNA transcript abundance	lung	6mo P3 saline-treated	6mo P3 ABE-treated	0.0069	Two-tailed	t=2.983 df=22
LMNA transcript abundance	Kidney	6mo P3 saline-treated	6mo P3 ABE-treated	0.0018	Two-tailed	t=3.543 df=22
LMNA transcript abundance	Spleen	6mo P3 saline-treated	6mo P3 ABE-treated	< 0.0001	Two-tailed	t=5.745 df=22

P14 6 month saline-treated versus P14 6 month ABE-treated ddPCR transcript abundance (Figure 3c, Extended Data Figure 4)

Progerin transcript abundance	Liver	6mo P14 saline-treated	6mo P14 ABE-treated	< 0.0001	Two-tailed	t=6.979 df=22
Progerin transcript abundance	Heart	6mo P14 saline-treated	6mo P14 ABE-treated	0.1325	Two-tailed	t=1.562 df=22
Progerin transcript abundance	Aorta	6mo P14 saline-treated	6mo P14 ABE-treated	0.9992	Two-tailed	t=0.0009725 df=16
Progerin transcript abundance	Quad	6mo P14 saline-treated	6mo P14 ABE-treated	< 0.0001	Two-tailed	t=5.741 df=22
Progerin transcript abundance	Bone	6mo P14 saline-treated	6mo P14 ABE-treated	0.2235	Two-tailed	t=1.261 df=18
Progerin transcript abundance	Skin	6mo P14 saline-treated	6mo P14 ABE-treated	0.6208	Two-tailed	t=0.5021 df=21
Progerin transcript abundance	Visc. Fat	6mo P14 saline-treated	6mo P14 ABE-treated	0.8041	Two-tailed	t=0.2512 df=21
Progerin transcript abundance	WAT	6mo P14 saline-treated	6mo P14 ABE-treated	0.0976	Two-tailed	t=1.759 df=16
Progerin transcript abundance	lung	6mo P14 saline-treated	6mo P14 ABE-treated	0.2897	Two-tailed	t=1.085 df=22
Progerin transcript abundance	Kidney	6mo P14 saline-treated	6mo P14 ABE-treated	0.2708	Two-tailed	t=1.130 df=22
Progerin transcript abundance	Spleen	6mo P14 saline-treated	6mo P14 ABE-treated	0.3053	Two-tailed	t=1.049 df=22
LMNA transcript abundance	Liver	6mo P14 saline-treated	6mo P14 ABE-treated	0.0015	Two-tailed	t=3.612 df=22
LMNA transcript abundance	Heart	6mo P14 saline-treated	6mo P14 ABE-treated	0.0013	Two-tailed	t=3.678 df=22
LMNA transcript abundance	Aorta	6mo P14 saline-treated	6mo P14 ABE-treated	0.0365	Two-tailed	t=2.282 df=16
LMNA transcript abundance	Quad	6mo P14 saline-treated	6mo P14 ABE-treated	0.1058	Two-tailed	t=1.687 df=22
LMNA transcript abundance	Bone	6mo P14 saline-treated	6mo P14 ABE-treated	0.379	Two-tailed	t=0.9019 df=18
LMNA transcript abundance	Skin	6mo P14 saline-treated	6mo P14 ABE-treated	0.6691	Two-tailed	t=0.4335 df=21
LMNA transcript abundance	Visc. Fat	6mo P14 saline-treated	6mo P14 ABE-treated	0.0357	Two-tailed	t=2.244 df=21
LMNA transcript abundance	WAT	6mo P14 saline-treated	6mo P14 ABE-treated	0.3739	Two-tailed	t=0.9148 df=16
LMNA transcript abundance	lung	6mo P14 saline-treated	6mo P14 ABE-treated	0.5735	Two-tailed	t=0.5715 df=22
LMNA transcript abundance	Kidney	6mo P14 saline-treated	6mo P14 ABE-treated	0.8876	Two-tailed	t=0.1430 df=22
LMNA transcript abundance	Spleen	6mo P14 saline-treated	6mo P14 ABE-treated	0.106	Two-tailed	t=1.686 df=22

P3 and P14 6 month saline-treated versus 6 month ABE-treated western blot analysis (Figure 3d, Extended Data Figure 5)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
Lamin A protein abundance	Liver (female)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0357	Two-tailed	t=2.426, df=10
Lamin A protein abundance	Liver (male)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0756	Two-tailed	t=1.982, df=10
Lamin A protein abundance	Liver (female)	6mo P14 saline-treated	6mo P14 ABE-treated	0.4152	Two-tailed	t=0.8501, df=10
Lamin A protein abundance	Liver (male)	6mo P14 saline-treated	6mo P14 ABE-treated	0.4378	Two-tailed	t=0.8082, df=10
Progerin protein abundance	Liver (female)	6mo P3 saline-treated	6mo P3 ABE-treated	<0.0001	Two-tailed	t=7.394, df=10
Progerin protein abundance	Liver (male)	6mo P3 saline-treated	6mo P3 ABE-treated	<0.0001	Two-tailed	t=7.636, df=10
Progerin protein abundance	Liver (female)	6mo P14 saline-treated	6mo P14 ABE-treated	0.0003	Two-tailed	t=5.530, df=10
Progerin protein abundance	Liver (male)	6mo P14 saline-treated	6mo P14 ABE-treated	0.00027	Two-tailed	t=5.476, df=10
Lamin A protein abundance	Heart (female)	6mo P3 saline-treated	6mo P3 ABE-treated	0.114	Two-tailed	t=1.732, df=10
Lamin A protein abundance	Heart (male)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0221	Two-tailed	t=2.706, df=10
Lamin A protein abundance	Heart (female)	6mo P14 saline-treated	6mo P14 ABE-treated	0.555	Two-tailed	t=0.6108, df=10
Lamin A protein abundance	Heart (male)	6mo P14 saline-treated	6mo P14 ABE-treated	0.3427	Two-tailed	t=0.9961, df=10
Progerin protein abundance	Heart (female)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0004	Two-tailed	t=5.129, df=10
Progerin protein abundance	Heart (male)	6mo P3 saline-treated	6mo P3 ABE-treated	<0.0001	Two-tailed	t=20.67, df=10
Progerin protein abundance	Heart (female)	6mo P14 saline-treated	6mo P14 ABE-treated	<0.0001	Two-tailed	t=7.658, df=10
Progerin protein abundance	Heart (male)	6mo P14 saline-treated	6mo P14 ABE-treated	<0.0001	Two-tailed	t=6.602, df=10
Lamin A protein abundance	Aorta (female)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0232	Two-tailed	t=2.731, df=9
Lamin A protein abundance	Aorta (male)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0031	Two-tailed	t=3.998, df=9
Lamin A protein abundance	Aorta (female)	6mo P14 saline-treated	6mo P14 ABE-treated	0.0109	Two-tailed	t=3.196, df=9
Lamin A protein abundance	Aorta (male)	6mo P14 saline-treated	6mo P14 ABE-treated	0.0003	Two-tailed	t=5.476, df=10
Progerin protein abundance	Aorta (female)	6mo P3 saline-treated	6mo P3 ABE-treated	0.0279	Two-tailed	t=2.616, df=9
Progerin protein abundance	Aorta (male)	6mo P3 saline-treated	6mo P3 ABE-treated	0.1966	Two-tailed	t=1.395, df=9
Progerin protein abundance	Aorta (female)	6mo P14 saline-treated	6mo P14 ABE-treated	0.0027	Two-tailed	t=4.099, df=9
Progerin protein abundance	Aorta (male)	6mo P14 saline-treated	6mo P14 ABE-treated	0.0203	Two-tailed	t=2.756, df=10

P3 and P14 6 month saline-treated versus 6 month ABE-treated VSMC counts and adventitial area (Figure 4b, Extended Data Figures 6,7)

Quantitation:	Tissue:	Sample 1:	Sample 2:	p-value:	Side:	t, df:
VSMC count in P3 samples	Aorta	6mo P3 saline-treated	6mo P3 ABE-treated	0.0188	Two-tailed	t=2.557 df=20
VSMC count in P14 samples	Aorta	6mo P14 saline-treated	6mo P14 ABE-treated	< 0.0001	Two-tailed	t=16.73 df=18
VSMC count in P3 samples	Aorta	6mo wild type untreated	6mo P3 ABE-treated	< 0.0001	Two-tailed	t=6.878 df=16
VSMC count in P14 samples	Aorta	6mo wild type untreated	6mo P14 ABE-treated	0.5719	Two-tailed	t=0.5772 df=16
Adventitial area count in P3 samples	Aorta	6mo P3 saline-treated	6mo P3 ABE-treated	0.3856	Two-tailed	t=0.8870 df=20
Adventitial area count in P14 samples	Aorta	6mo P14 saline-treated	6mo P14 ABE-treated	< 0.0001	Two-tailed	t=7.810 df=18
Adventitial area count in P3 samples	Aorta	6mo wild type untreated	6mo P3 ABE-treated	0.004	Two-tailed	t=3.363 df=16
Adventitial area count in P14 samples	Aorta	6mo wild type untreated	6mo P14 ABE-treated	0.8823	Two-tailed	t=0.1504 df=16

Supplementary References

64 Babcock, V. I. & Southam, C. M. Obstructive uropathy in laboratory mice. *Proc Soc Exp Biol Med* **120**, 580-581, doi:10.3181/00379727-120-30595 (1965).

Additional relevant references on HGPS

- Merideth, M. A. *et al.* Phenotype and course of Hutchinson-Gilford progeria syndrome. *N Engl J Med* **358**, 592-604, doi:10.1056/NEJMoa0706898 (2008).
- DeBusk, F. L. The Hutchinson-Gilford progeria syndrome: report of 4 cases and review of the literature. *The Journal of pediatrics* (1972).
- Hennekam, R. C. Hutchinson-Gilford progeria syndrome: review of the phenotype. *Am J Med Genet A* **140**, 2603-2624, doi:10.1002/ajmg.a.31346 (2006).
- Goldman, R. D. *et al.* Accumulation of mutant lamin A causes progressive changes in nuclear architecture in Hutchinson-Gilford progeria syndrome. *Proc Natl Acad Sci U S A* **101**, 8963-8968, doi:10.1073/pnas.0402943101 (2004).
- Cao, K., Capell, B. C., Erdos, M. R., Djabali, K. & Collins, F. S. A lamin A protein isoform overexpressed in Hutchinson-Gilford progeria syndrome interferes with mitosis in progeria and normal cells. *Proc Natl Acad Sci U S A* **104**, 4949-4954, doi:10.1073/pnas.0611640104 (2007).
- Glynn, M. W. & Glover, T. W. Incomplete processing of mutant lamin A in Hutchinson-Gilford progeria leads to nuclear abnormalities, which are reversed by farnesyltransferase inhibition. *Hum Mol Genet* **14**, 2959-2969, doi:10.1093/hmg/ddi326 (2005).
- Capell, B. C. *et al.* A farnesyltransferase inhibitor prevents both the onset and late progression of cardiovascular disease in a progeria mouse model. *Proc Natl Acad Sci U S A* **105**, 15902-15907, doi:10.1073/pnas.0807840105 (2008).
- Capell, B. C. *et al.* Inhibiting farnesylation of progerin prevents the characteristic nuclear blebbing of Hutchinson-Gilford progeria syndrome. *Proc Natl Acad Sci U S A* **102**, 12879-12884, doi:10.1073/pnas.0506001102 (2005).
- Yang, S. H., Qiao, X., Fong, L. G. & Young, S. G. Treatment with a farnesyltransferase inhibitor improves survival in mice with a Hutchinson-Gilford progeria syndrome mutation. *Biochim Biophys Acta* **1781**, 36-39, doi:10.1016/j.bbalip.2007.11.003 (2008).
- Yang, S. H. *et al.* A farnesyltransferase inhibitor improves disease phenotypes in mice with a Hutchinson-Gilford progeria syndrome mutation. *J Clin Invest* **116**, 2115-2121, doi:10.1172/JCI28968 (2006).
- Yang, S. H. *et al.* Blocking protein farnesyltransferase improves nuclear blebbing in mouse fibroblasts with a targeted Hutchinson-Gilford progeria syndrome mutation. *Proc Natl Acad Sci U S A* **102**, 10291-10296, doi:10.1073/pnas.0504641102 (2005).
- Toth, J. I. *et al.* Blocking protein farnesyltransferase improves nuclear shape in fibroblasts from humans with progeroid syndromes. *Proc Natl Acad Sci U S A* **102**, 12873-12878, doi:10.1073/pnas.0505767102 (2005).
- Mallampalli, M. P., Huyer, G., Bendale, P., Gelb, M. H. & Michaelis, S. Inhibiting farnesylation reverses the nuclear morphology defect in a HeLa cell model for Hutchinson-Gilford progeria syndrome. *Proc Natl Acad Sci U S A* **102**, 14416-14421, doi:10.1073/pnas.0503712102 (2005).
- Fong, L. G. *et al.* A protein farnesyltransferase inhibitor ameliorates disease in a mouse model of progeria. *Science* **311**, 1621-1623, doi:10.1126/science.1124875 (2006).

- Varela, I. *et al.* Combined treatment with statins and aminobisphosphonates extends longevity in a mouse model of human premature aging. *Nat Med* **14**, 767-772, doi:10.1038/nm1786 (2008).
- Cao, K. *et al.* Progerin and telomere dysfunction collaborate to trigger cellular senescence in normal human fibroblasts. *J Clin Invest* **121**, 2833-2844, doi:10.1172/JCI43578 (2011).
- Cenni, V. *et al.* Autophagic degradation of farnesylated prelamin A as a therapeutic approach to lamin-linked progeria. *European journal of histochem* (2011).
- Lee, J. M. *et al.* Modulation of *LMNA* splicing as a strategy to treat prelamin A diseases. *J Clin Invest* **126**, 1592-1602, doi:10.1172/JCI85908 (2016).
- Cao, K. *et al.* Rapamycin reverses cellular phenotypes and enhances mutant protein clearance in Hutchinson-Gilford progeria syndrome cells. *Sci Transl Med* **3**, 89ra58, doi:10.1126/scitranslmed.3002346 (2011).
- Balmus, G. *et al.* Targeting of NAT10 enhances healthspan in a mouse model of human accelerated aging syndrome. *Nat Commun* **9**, 1700, doi:10.1038/s41467-018-03770-3 (2018).
- Lee, S. J. *et al.* Interruption of progerin-lamin A/C binding ameliorates Hutchinson-Gilford progeria syndrome phenotype. *J Clin Invest* **126**, 3879-3893, doi:10.1172/JCI84164 (2016).

Additional relevant references on base editing

- Komor, A. C., Kim, Y. B., Packer, M. S., Zuris, J. A. & Liu, D. R. Programmable editing of a target base in genomic DNA without double-stranded DNA cleavage. *Nature* **533**, 420-424, doi:10.1038/nature17946 (2016).
- Yeh, W. H., Chiang, H., Rees, H. A., Edge, A. S. B. & Liu, D. R. *In vivo* base editing of post-mitotic sensory cells. *Nat Commun* **9**, 2184, doi:10.1038/s41467-018-04580-3 (2018).
- Huang, T. P. *et al.* Circularly permuted and PAM-modified Cas9 variants broaden the targeting scope of base editors. *Nat Biotechnol* **37**, 626-631, doi:10.1038/s41587-019-0134-y (2019).
- Kleinstiver, B. P. *et al.* Engineered CRISPR-Cas9 nucleases with altered PAM specificities. *Nature* **523**, 481-485, doi:10.1038/nature14592 (2015).
- Hirano, S., Nishimasu, H., Ishitani, R. & Nureki, O. Structural Basis for the Altered PAM Specificities of Engineered CRISPR-Cas9. *Mol Cell* **61**, 886-894, doi:10.1016/j.molcel.2016.02.018 (2016).
- Nishida, K. *et al.* Targeted nucleotide editing using hybrid prokaryotic and vertebrate adaptive immune systems. *Science* **353**, doi:10.1126/science.aaf8729 (2016).
- Grunewald, J. *et al.* CRISPR DNA base editors with reduced RNA off-target and self-editing activities. *Nat Biotechnol* **37**, 1041-1048, doi:10.1038/s41587-019-0236-6 (2019).
- Grunewald, J. *et al.* Transcriptome-wide off-target RNA editing induced by CRISPR-guided DNA base editors. *Nature* **569**, 433-437, doi:10.1038/s41586-019-1161-z (2019).
- Rees, H. A., Wilson, C., Doman, J. L. & Liu, D. R. Analysis and minimization of cellular RNA editing by DNA adenine base editors. *Sci Adv* **5**, eaax5717, doi:10.1126/sciadv.aax5717 (2019).

- Zhou, C. *et al.* Off-target RNA mutation induced by DNA base editing and its elimination by mutagenesis. *Nature* **571**, 275-278, doi:10.1038/s41586-019-1314-0 (2019).
- Jin, S. *et al.* Cytosine, but not adenine, base editors induce genome-wide off-target mutations in rice. *Science* **364**, 292-295, doi:10.1126/science.aaw7166 (2019).
- Zuo, E. *et al.* Cytosine base editor generates substantial off-target single-nucleotide variants in mouse embryos. *Science* **364**, 289-292, doi:10.1126/science.aav9973 (2019).
- Doman, J. L., Raguram, A., Newby, G. A. & Liu, D. R. Evaluation and minimization of Cas9-independent off-target DNA editing by cytosine base editors. *Nat Biotechnol*, doi:10.1038/s41587-020-0414-6 (2020).

Additional relevant references on RNA editing and AAV-induced liver tumors

- Bass, B. L. RNA editing by adenosine deaminases that act on RNA. *Annual review of biochemistry* (2002)
- Bell, P., Moscioni, A. D., McCarter, R. J., Wu, D. & Therapy, G.-G. Analysis of tumors arising in male B6C3F1 mice with and without AAV vector delivery to liver. *Molecular Therapy* (2006).