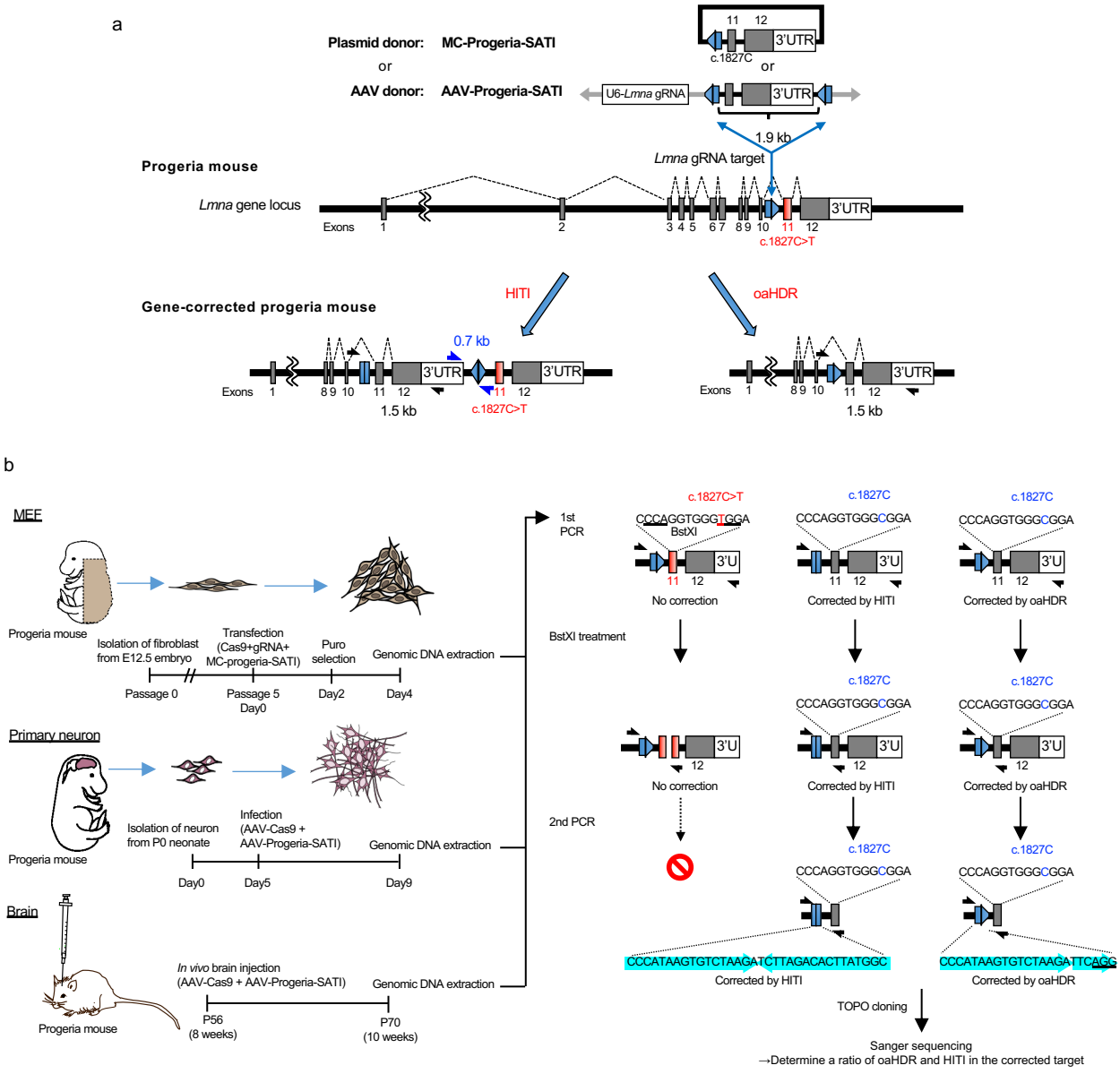
a
Plasmid donor: MC-Progeria-SATI
or
AAV donor: AAV-Progeria-SATI
11 12
3'UTR
c.1827C
or
U6-Lmna gRNA
1.9 kb
Lmna gRNA target
Progeria mouse
Lmna gene locus
Exons
c.1827C>T
HITI
oaHDR
Gene-corrected progeria mouse
0.7 kb
1.5 kb
b
MEE
Progeria mouse
Isolation of fibroblast from E12.5 embryo
Transfection (Cas9+gRNA+ MC-progeria-SATI)
Puro selection
Genomic DNA extraction
Passage 0
Passage 5
Day0
Day2
Day4
Primary neuron
Isolation of neuron from P0 neonate
Infection (AAV-Cas9 + AAV-Progeria-SATI)
Day0
Day5
Day9
Brain
In vivo brain injection (AAV-Cas9 + AAV-Progeria-SATI)
P56 (8 weeks)
P70 (10 weeks)
1st PCR
BstXI treatment
2nd PCR
CCCAGGTGGGTGGA
BstXI
No correction
CCCAGGTGGGCGGA
Corrected by HITI
Corrected by oaHDR
CCCATAAGTGTCTAAGATCTTAGACACTTATGGC
CCCATAAGTGTCTAAGATTCAGG
TOPO cloning
Sanger sequencing
→Determine a ratio of oaHDR and HITI in the corrected target

Supplementary Figure S8 | Experimental design for oaHDR- or HITI-mediated gene knock-in profile after SATI-mediated gene-correction of progeria mice *in vitro* and *in vivo*. a Schematic representation of the *Lmna*^{G609G} (c.1827C>T) gene correction with plasmid (MC-Progeria-SATI) or AAV (AAV-Progeria-SATI) carrying SATI-mediated gene-correction donor. After gene correction mediated by NHEJ-mediated HITI, targeted sequence including corrected mutation are inserted in intron 10, just in front of mutated exon 11 (left). After gene correction mediated by oaHDR, the mutation is corrected with no change of other genomic sequence except for point mutation (right). Blue pentagon, *Lmna* intron 10 gRNA target sequence. A Black line within blue pentagon, Cas9 cleavage site. Blue half-arrows, PCR primers for detecting only HITI. Black half-arrows, PCR primers for detecting junction site of gene correction. **b** Experimental scheme for evaluation of corrected gene sequence. Genomic DNA is extracted from progeria MEF, primary neuron, and brain tissue, respectively. To enrich the corrected sequence, BstXI enzyme digestion which can recognize only uncorrected mutation is performed between 1st PCR and 2nd PCR. Final PCR product are cloned into TOPO cloning vector and sequenced to determine the ratio of HITI and oaHDR.