

Table S1. Mutation rate estimates for hgRNAs in the MARC1 mice. Related to **Figures 4 and 5.**

hgRNA identifier	Mutation rate (muts / day)			
	Posterior mean estimate	Lower bound (90% CI)	Higher bound (90% CI)	Naïve estimate
AAGCCGCGCG	5.08E-02	3.60E-02	9.28E-02	6.69E-02
ACATTCGGTT	6.31E-04	6.31E-04	8.90E-04	1.96E-03
ACCACTGCTG	6.31E-04	6.31E-04	8.90E-04	9.81E-03
ACCCTGGGAC	6.31E-04	6.31E-04	8.90E-04	2.85E-03
ACTCCATGTT	6.31E-04	6.31E-04	1.06E-03	5.32E-03
AGCACACCCA	1.01E-01	7.17E-02	1.31E-01	1.49E-01
AGGTGTTCAA	4.28E-02	3.03E-02	6.58E-02	5.46E-02
AGTCTGCCTC	6.31E-04	6.31E-04	1.06E-03	4.81E-03
ATGACCCACC	6.31E-04	6.31E-04	1.06E-03	6.92E-04
ATGCTTAGCT	1.08E-02	7.65E-03	1.40E-02	1.62E-02
ATGGAGGGAC	4.01E-01	2.84E-01	6.16E-01	1.88E+00
ATGGCGCCTA	6.31E-04	6.31E-04	8.90E-04	6.19E-03
ATGTCATCGA	2.01E-01	2.01E-01	3.68E-01	9.67E-01
CAAGGGCCCT	1.20E-01	8.52E-02	1.56E-01	1.57E-01
CACAACGCCC	4.76E-01	2.84E-01	5.19E-01	2.11E+00
CACCTCGGAC	2.15E-02	1.81E-02	3.31E-02	8.05E-02
CACTCTCAAG	4.76E-01	4.01E-01	7.32E-01	2.77E+00
CATATATTCC	2.01E-01	1.70E-01	3.10E-01	7.64E-01
CATCGTCGTC	6.31E-04	6.31E-04	8.90E-04	1.02E-03
CATTGGAGGT	1.70E-01	1.43E-01	3.10E-01	6.34E-01
CCACCATCCG	1.08E-02	9.09E-03	1.66E-02	2.42E-02
CCCAAACAC	1.01E-01	8.52E-02	1.56E-01	1.43E-01
CCGTACTTCA	1.70E-01	1.43E-01	2.61E-01	4.36E-01
CCTTTACCGC	6.31E-04	6.31E-04	8.90E-04	2.65E-03
CGAATCCTTT	6.31E-04	6.31E-04	1.06E-03	4.99E-03
CGACAGTTAT	6.31E-04	6.31E-04	1.06E-03	6.47E-03
CGGGGGTTCC	8.52E-02	6.04E-02	1.10E-01	2.74E-01
CGGTCTGTAC	1.63E-03	1.37E-03	2.50E-03	5.70E-03
CGTAGGGCCC	2.15E-02	1.81E-02	3.31E-02	5.78E-02
CGTGTTGTCT	9.70E-04	9.70E-04	1.77E-03	5.62E-03
CTACTCGGCC	1.20E-01	8.52E-02	1.56E-01	1.40E-01
CTCGTAAGTC	4.76E-01	2.84E-01	5.19E-01	2.17E+00
CTGAGTTTTA	1.63E-03	1.63E-03	2.97E-03	1.05E-01
CTGCTATCGA	7.17E-02	7.17E-02	1.31E-01	2.24E-01
CTTTTGTCGG	6.31E-04	6.31E-04	1.06E-03	2.47E-03

GAAGACCCGC	1.52E-02	1.28E-02	2.78E-02	2.92E-02
GACACAGACA	1.20E-01	1.20E-01	2.19E-01	2.57E-01
GACCCTTCCT	4.28E-02	3.60E-02	6.58E-02	1.40E-01
GACGAAGACA	3.03E-02	2.55E-02	4.66E-02	4.39E-02
GATACCCCA	1.20E-01	1.20E-01	2.19E-01	5.68E-01
GCCAACGAGC	6.31E-04	6.31E-04	8.90E-04	2.42E-03
GCCAAGATGG	6.31E-04	6.31E-04	1.06E-03	3.72E-03
GCCCAGATAC	6.88E-04	6.88E-04	1.26E-03	9.27E-04
GCGTCGCCCT	3.03E-02	3.03E-02	5.54E-02	5.01E-02
GCTCTACGCC	6.31E-04	6.31E-04	1.06E-03	4.67E-03
GGCCCCTACA	6.31E-04	6.31E-04	8.90E-04	1.20E-03
GGCGACCGCA	5.42E-03	5.42E-03	9.91E-03	1.13E-02
GGGTGACACG	6.31E-04	6.31E-04	8.90E-04	9.73E-03
GTACACAATT	1.43E-01	1.43E-01	2.61E-01	5.32E-01
GTCAAATACC	1.63E-03	9.70E-04	1.77E-03	8.02E-03
GTGGAGCCTC	1.13E+00	6.72E-01	1.23E+00	3.01E+00
TAACTTATAC	6.31E-04	6.31E-04	1.06E-03	1.53E-03
TACACAGATA	8.52E-02	6.04E-02	1.10E-01	2.29E-01
TACACCCAC	4.28E-02	4.28E-02	7.82E-02	6.30E-02
TAGAACCATG	3.60E-02	3.03E-02	5.54E-02	5.35E-02
TAGCCATGCA	1.37E-03	9.70E-04	1.77E-03	5.63E-03
TCATCAGGCC	2.39E-01	2.01E-01	3.68E-01	1.31E+00
TCTATCGAGG	6.31E-04	6.31E-04	8.90E-04	1.28E-02
TCTTATAACC	7.17E-02	5.08E-02	9.28E-02	1.13E-01
TGGTGATGGT	6.72E-01	4.76E-01	8.70E-01	2.67E+00
TTAGCTATGT	9.48E-01	6.72E-01	1.23E+00	2.82E+00
TTATCGTTCA	6.31E-04	6.31E-04	8.90E-04	1.70E-03
TTGAGCATAA	1.13E+00	4.01E-01	1.73E+00	2.86E+00
TTGTGACATA	1.63E-03	1.63E-03	2.97E-03	8.73E-03

Table S2. hgRNA identifier, spacer sequences and mutation rate estimates in the iPSC line. hgRNA #22 was not targeted by amplification primers. Related to **Figure 7**.

hgRNA #	Identifier	Spacer	Mutation rate estimates (mut / day)
1	AAACCCATGA	GGTTTAGTATGGAGGGAAGTG	0.059413881
2	AACATGCTAG	GGTTTTCGATCATAGGTCGTG	0.006335047
3	AATAATGCCG	GGTGCCCTTTATGGGACCGTG	0.000591681
4	AATCCATCAC	GGTGACAAACGTATGTCAGTG	0.019481606

5	AATTGGGCAA	GGTTGTGGGGAAGCTCGGTGTG	-1.55303E-11
6	AGACAGCAAC	GGTGTCTTTGCTCGAGGGTG	0.00032599
7	ATACCACACT	GGTTGTAAGCGATGGTTTGTG	-1.55303E-11
8	ATCTAACCGA	GGTGTGCGGAGATTATGCGTG	-1.55303E-11
9	ATGACCGTCG	GGTCCTAGAAGCTGAGTTGTG	0.120838624
10	CAACGAGATT	GGTGCTAGCGGTTTCGAAGTG	0.029447842
11	CATTCACAAA	GGTGGCAATTTCGATCTGAGTG	0.008819366
12	CCCCGCCGCC	GGTAGAATGGATCCACGGGTG	0.008408573
13	CCCTCGCACC	GGTTCAACCGGCGTCTTTGTG	0.135938928
14	CCGTTAACAC	GGTTGGCTTTACTCCTTTGTG	0.019492236
15	CGGCGGGTTG	GGTCGTCGTTTCGTAGGGCGTG	0.023817137
16	CGTTCATCAA	GGTGAGAACAGAACGTTTTGG	0.04235805
17	GAATCAGCCG	GGTTTTAGTAAATGGTGAGTG	0.020988445
18	GAATTA AAAA	GGTGCTAATAGTTAGCTCGTG	0.008158287
19	GACAACCTCC	GGTAATCTAAAGATCCCCGTG	-1.55303E-11
20	GACTATGTAA	GGTACTAGTTACTTACGGGTG	-1.55303E-11
21	GAGTCAAGCG	GGTTATCGTTACGGATTTGTG	0.039817255
22	GCCAAAAGCT	GGTGGTCGCCGTGGAGAGGTG	NA
23	GGCAACTACG	GGTGGCAGCCAGCCACTTGTG	0.00571604
24	GTAATATATA	GGTGAGCATGATAACGTCGTG	0.059595844
25	GTGGGCGAGA	GGTGAGATGCCTCAAGTGGTG	0.217232375
26	TAAACCCAAT	GGTTTACTTAGTTAACTAGTG	0.008963861
27	TAATTAATCC	GGTTGAGATAATCAAAAAGTG	0.029885995
28	TCAACCCTCT	GGTGACGCGAGGACGGTGGTG	0.024973171
29	TCAGCAAAAA	GGTG (truncated)	0.001174739
30	TGCACTTCCT	GGTTCCCGTTAGCTCGTAGTG	0.048665863
31	TGTCCAGATT	GGTCTTCCTGGAATCTACGTG	0.068354208
32	TTCTTCTCCC	GGTCGCGAAAATGTGCCGGTG	0.011352671

Table S3. Oligonucleotides used in this study. Related to **Figure 7**.

Oligonucleotide	Sequence	Source
AAVS1 guide RNA	CACCGGGGCCACTAGGGACAGGAT	Eldred et al. ⁴⁵
AAVS1 right homology arm genotyping reverse primer	GGAACGGGGCTCAGTCTGA	Eldred et al. ⁴⁵
ACTB qPCR forward primer	GCGAGAAGATGACCCAGATC	Wahlin et al. ⁴⁶
ACTB qPCR reverse primer	CCAGTGGTACGGCCAGAGG	Wahlin et al. ⁴⁶
Cas9 genotyping forward primer	CACCTTGTACTCGTCGGTGA	Eldred et al. ⁴⁵

Cas9 qPCR forward primer	CCGAAGAGGTCGTGAAGAAG	González et al. ⁴⁷
Cas9 qPCR reverse primer	GCCTTATCCAGTTCGCTCAG	González et al. ⁴⁷
CREBBP qPCR forward primer	GAGAGCAAGCAAACGGAGAG	Wahlin et al. ⁴⁶
CREBBP qPCR reverse primer	AAGGGAGGCCAAACAGGACA	Wahlin et al. ⁴⁶
GAPDH qPCR forward primer	TAGCCAAATTCGTTGTCATACC	Maruotti et al. ⁴⁸
GAPDH qPCR reverse primer	CTGACTTCAACAGCGACACC	Maruotti et al. ⁴⁸
hgRNA PCR1 forward primer	ACACTCTTTCCCTACACGACGCTCTTCCGATC TATGGACTATCATATGCTTACCGT	Leeper et al. ³⁰
hgRNA PCR1 reverse primer	TGACTGGAGTTCAGACGTGTGCTCTTCCGATC TGCCATACCAATGGGCCCGAA	Leeper et al. ³⁰
hgRNA PCR1 truncated forward primer	CTACACTCTTTCCCTACACGAC	Leeper et al. ³⁰
hgRNA PCR1 truncated reverse primer	GTGACTGGAGTTCAGACGTG	Leeper et al. ³⁰
hgRNA pre-amplification forward primer	AAGTAATAATTTCTTGGGTAGTTTGCAG	Leeper et al. ³⁰
hgRNA pre-amplification reverse primer	GAAAAAGCCATACCAATGGGC	Leeper et al. ³⁰
hgRNA qPCR forward primer	ATGGACTATCATATGCTTACCGT	Kalhor et al. ²⁹
hgRNA qPCR reverse primer	TTCAAGTTGATAACGGACTAGC	Kalhor et al. ²⁹
rtTA genotyping forward primer	GCTGATTATGATCCTGCAAGC	Eldred et al. ⁴⁵
rtTA qPCR forward primer	GCTAAAGTGCATCTCGGCAC	This paper
rtTA qPCR reverse primer	TGTTCCCTCCAATACGCAGCC	This paper
Sox11 qPCR forward primer	TGATGTTTCGACCTGAGCTTG	Remeseiro et al. ⁴⁹
Sox11 qPCR reverse primer	TAGTCGGGGAACCTCGAAGTG	Remeseiro et al. ⁴⁹