

**Supplementary Table S1 Top ten genome-wide off-target sites used in this study**

	Sequence	Score	Mismatches	Locus
OT1	GGCTGTGGAGTGCATGTGCGA <u>AAGGT</u>	5.0	2MMs [8:10]	chr10:-79469902
OT2*	TGCATTGTAATGCATGTGCAC <u>CAGGG</u>	0.7	4MMs [1:4:5:20]	chr13:-12962821
OT2*	TGCATTGTAATGCATGTGCAC <u>CAGGG</u>	0.7	4MMs [1:4:5:20]	chr13:-13174810
OT2*	TGCATTGTAATGCATGTGCAC <u>CAGGG</u>	0.7	4MMs [1:4:5:20]	chr13:+13206983
OT2*	TGCATTGTAATGCATGTGCAC <u>CAGGG</u>	0.7	4MMs [1:4:5:20]	chr13:-27869407
OT3	TGCAGTGTAGTGCATGTGCAC <u>CAGGG</u>	0.7	4MMs [1:4:10:20]	chr4:-152973806
OT4	GACTGTGCACTGCATGTGCC <u>AGGGT</u>	0.6	4MMs [2:8:10:20]	chr1:-134765564
OT5	GGCAATGCAATGCATGTGAGT <u>GGTC</u>	0.5	4MMs [4:5:8:19]	chr9:-115822056
OT6	GCGTGTGTGAGGCATGTGCG <u>AGGCA</u>	0.5	4MMs [2:3:9:11]	chr15:-99017711
OT7	GCCTGTGCAGTGCATGTGTG <u>GAGAC</u>	0.5	4MMs [2:8:10:19]	chr1:+94173408

Off-target sites were predicted using the CRISPR Design server (<http://crispr.mit.edu>). Ten sites were chosen based on sequence similarity. PAM sequences are underlined.

\*Duplicated region in the annotated mouse genome.