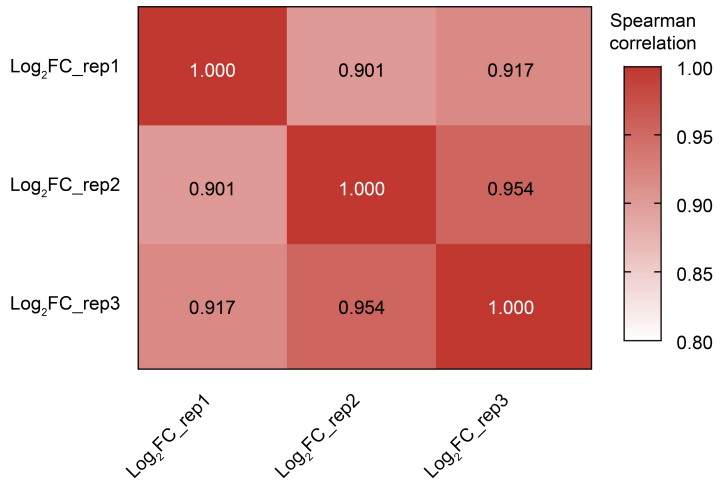
Supplementary information

PIVOT: A hyper-compact, PAM-independent TIGR-Tas editor enabling efficient *in vivo* gene editing via AAV and LNP delivery

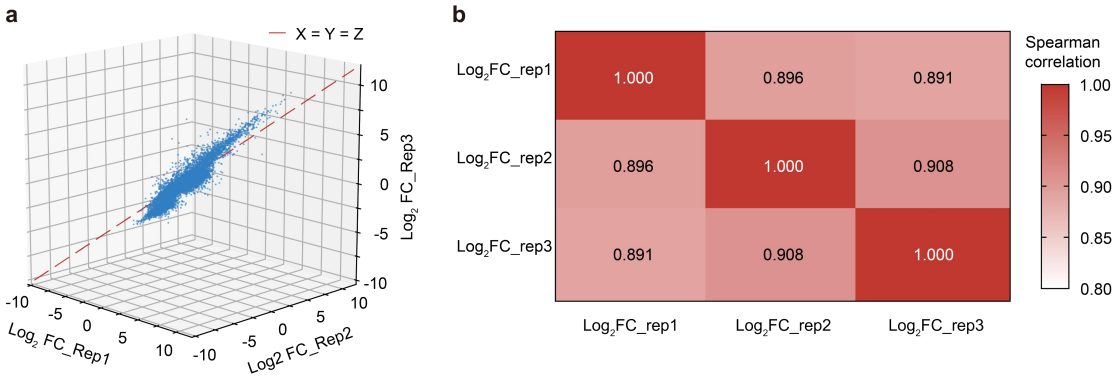
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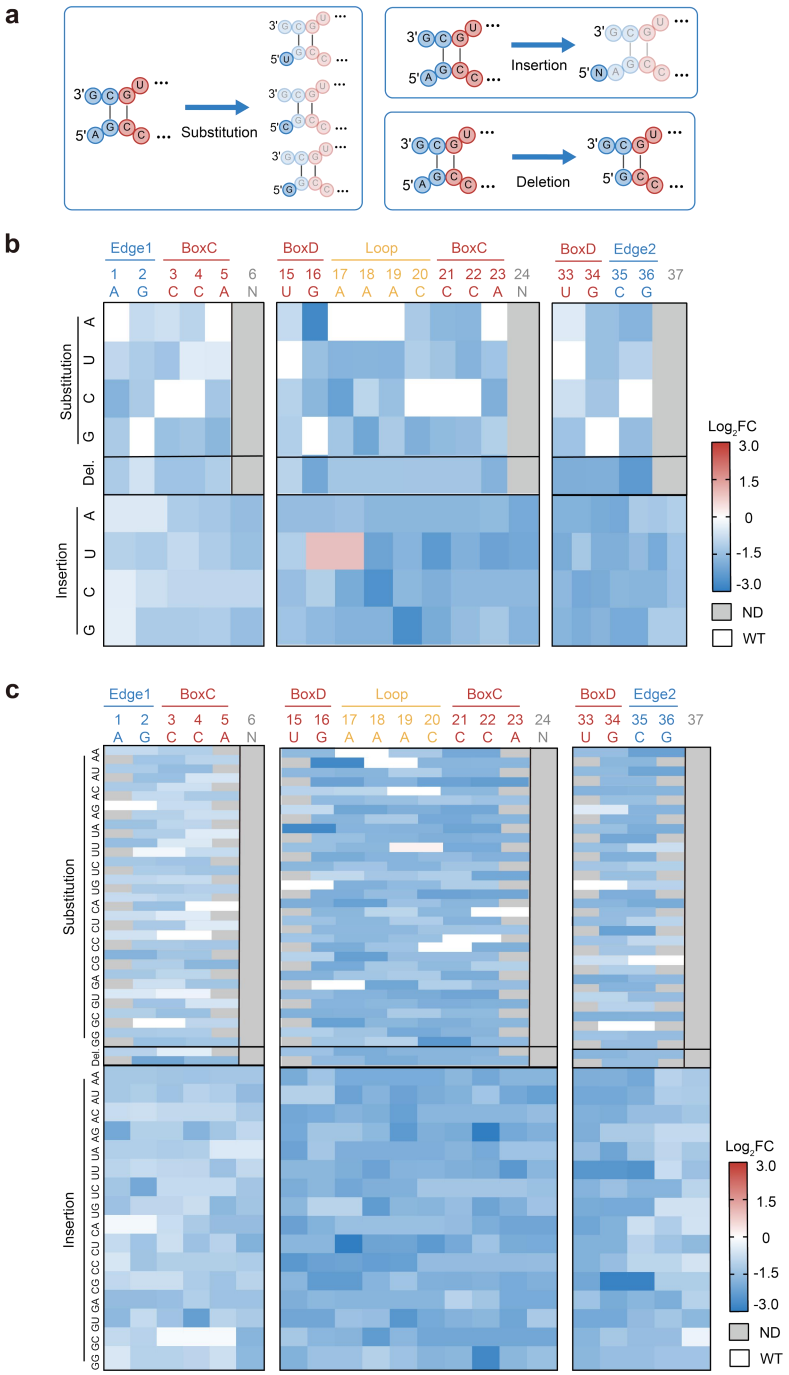
Supplementary Tables 1-4



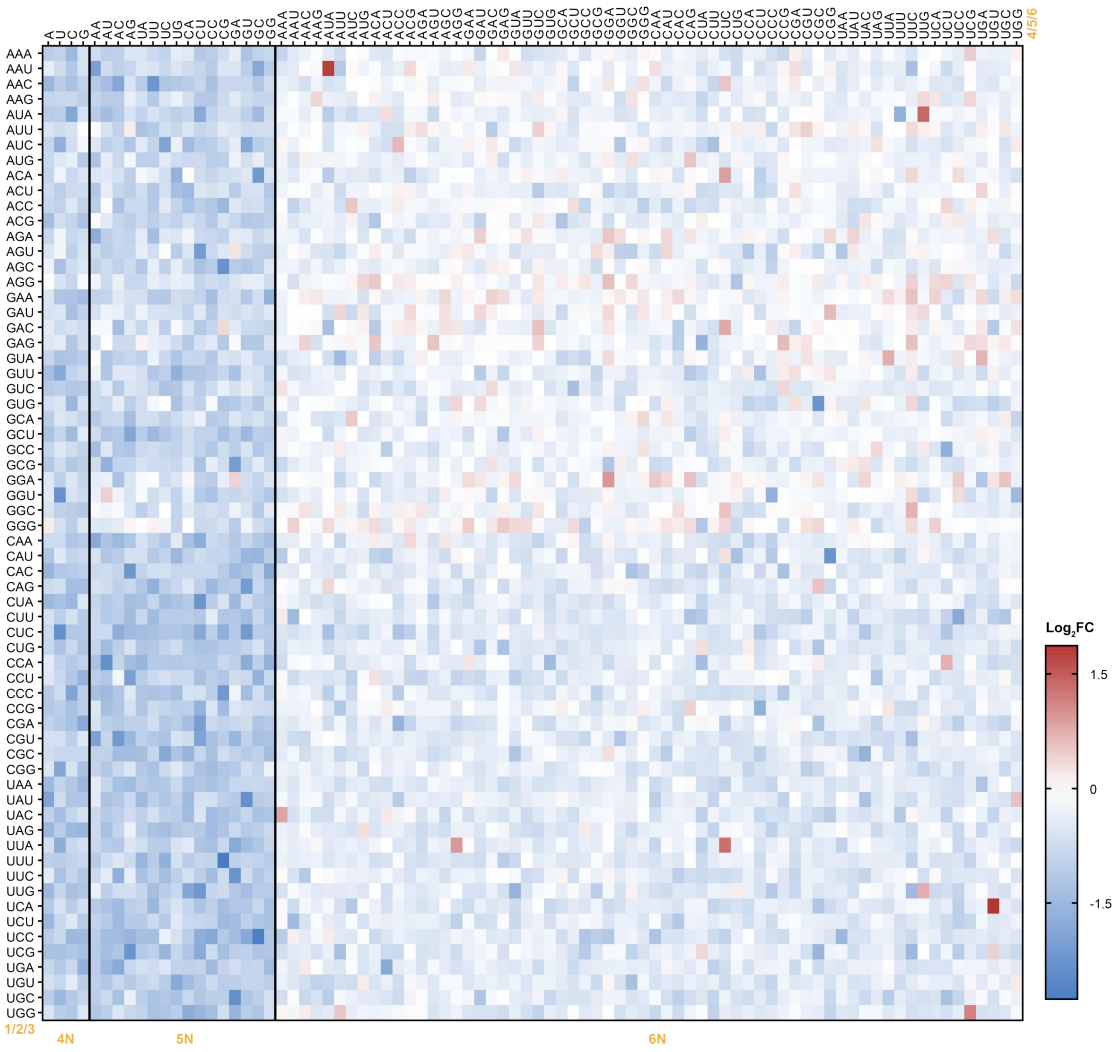
Supplementary Figure 1 | Inter-replicate reproducibility of the ParTasR deep mutational scanning screen. Pairwise Spearman correlation coefficients of Log_2FC enrichment values among three independent replicates. Spearman correlation assesses the consistency of variant enrichment rankings across screens, with high values indicating robust reproducibility.



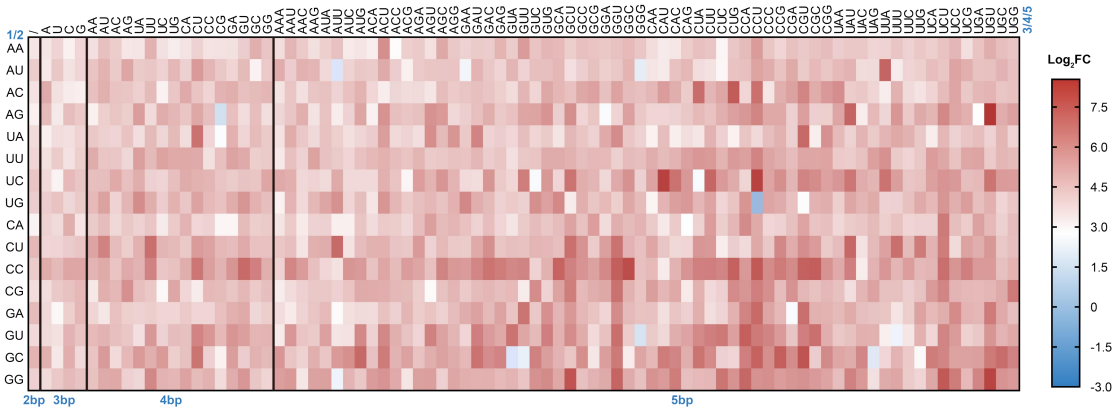
Supplementary Figure 2 | Inter-replicate reproducibility of the tigRNA scaffold DMS screen. a, Three-dimensional scatter plot depicting Log_2FC enrichment values for all tigRNA variants across three independent replicates; the diagonal line represents equivalence of Log_2FC values across replicates. **b,** Heat map showing pairwise Spearman rank correlation coefficients of Log_2FC values among the three replicates.



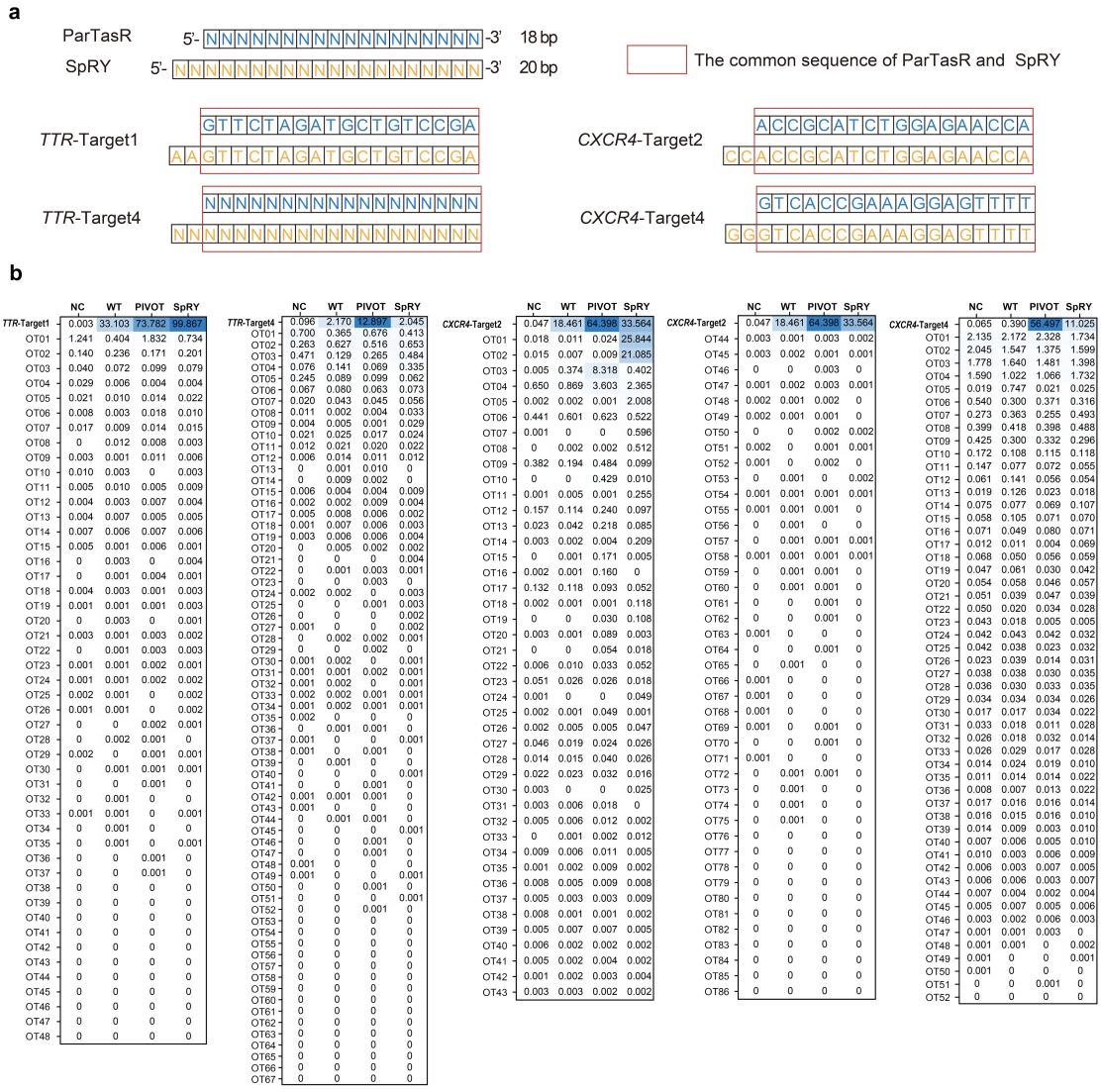
Supplementary Figure 3 | Systematic mutational scanning of the tigRNA scaffold. **a,** Schematic of the mutagenesis strategy, showing single-nucleotide and consecutive double-nucleotide substitutions, deletions, and insertions across the full-length tigRNA scaffold. **b,** Mean Log_2FC values for single-nucleotide substitutions, deletions, and insertions across the tigRNA scaffold. **c,** Mean Log_2FC values for consecutive double-nucleotide substitutions, deletions, and insertions across the tigRNA scaffold. Values are derived from three independent replicates.



Supplementary Figure 4 | Deep mutational scanning of the tigRNA central loop. Heat map of mean Log_2FC enrichment values for central loop variants with loop lengths of 4, 5, and 6 nt from three independent replicates. Each tile represents a distinct loop sequence.



Supplementary Figure 5 | Deep mutational scanning of tigRNA terminal stem extensions. Heat map of mean Log_2FC enrichment values for variants with 2–5 bp paired terminal stem extensions from three independent replicates



	NC	WT	PIVOT	SpRY
TTR-Target1	0.003	33.103	73.762	99.867
OT01	1.241	0.404	1.832	0.734
OT02	0.140	0.236	0.171	0.201
OT03	0.040	0.072	0.099	0.079
OT04	0.029	0.006	0.004	0.004
OT05	0.021	0.010	0.014	0.022
OT06	0.008	0.003	0.018	0.010
OT07	0.017	0.009	0.014	0.015
OT08	0	0.012	0.008	0.003
OT09	0.003	0.001	0.011	0.006
OT10	0.010	0.003	0	0.003
OT11	0.005	0.010	0.005	0.009
OT12	0.004	0.003	0.007	0.004
OT13	0.004	0.007	0.005	0.005
OT14	0.007	0.006	0.007	0.006
OT15	0.005	0.001	0.006	0.001
OT16	0	0.003	0	0.004
OT17	0	0.001	0.004	0.001
OT18	0.004	0.003	0.001	0.003
OT19	0.001	0.001	0.001	0.003
OT20	0	0.003	0	0.001
OT21	0.003	0.001	0.003	0.002
OT22	0	0.001	0.003	0.003
OT23	0.001	0.001	0.002	0.001
OT24	0.001	0.001	0.002	0.002
OT25	0.002	0.001	0	0.002
OT26	0.001	0.001	0	0.002
OT27	0	0	0.002	0.001
OT28	0	0.002	0.001	0
OT29	0.002	0	0.001	0.001
OT30	0	0.001	0.001	0.001
OT31	0	0	0.001	0
OT32	0	0.001	0	0
OT33	0.001	0.001	0	0.001
OT34	0	0.001	0	0
OT35	0	0.001	0	0.001
OT36	0	0	0.001	0
OT37	0	0	0.001	0
OT38	0	0	0	0
OT39	0	0	0	0
OT40	0	0	0	0
OT41	0	0	0	0
OT42	0	0	0	0
OT43	0	0	0	0
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OT48	0	0	0	0

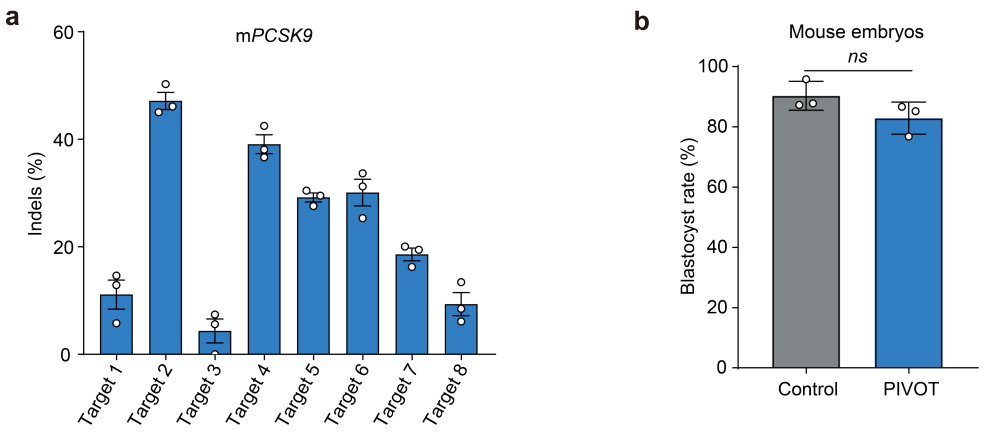
	NC	WT	PIVOT	SpRY
TTR-Target4	0.096	2.170	12.897	2.045
OT01	0.700	0.365	0.676	0.413
OT02	0.263	0.627	0.516	0.653
OT03	0.471	0.129	0.265	0.484
OT04	0.076	0.141	0.069	0.335
OT05	0.245	0.089	0.099	0.062
OT06	0.067	0.080	0.063	0.073
OT07	0.020	0.043	0.045	0.056
OT08	0.011	0.002	0.004	0.033
OT09	0.004	0.005	0.001	0.029
OT10	0.021	0.025	0.017	0.024
OT11	0.012	0.021	0.020	0.022
OT12	0.006	0.014	0.011	0.012
OT13	0	0.001	0.010	0
OT14	0	0.009	0.002	0
OT15	0.006	0.004	0.004	0.009
OT16	0.002	0.002	0.009	0.004
OT17	0.005	0.008	0.006	0.002
OT18	0.001	0.007	0.006	0.003
OT19	0.003	0.006	0.006	0.004
OT20	0	0.005	0.002	0.002
OT21	0	0	0	0.004
OT22	0	0.001	0.003	0.001
OT23	0	0	0.003	0
OT24	0.002	0.002	0	0.003
OT25	0	0	0.001	0.003
OT26	0	0	0	0.002
OT27	0.001	0	0	0.002
OT28	0	0.002	0.002	0.001
OT29	0	0	0.002	0
OT30	0.001	0.002	0	0.001
OT31	0.001	0.001	0.002	0.001
OT32	0.001	0.002	0	0.001
OT33	0.002	0.002	0.001	0.001
OT34	0.001	0.002	0.001	0.001
OT35	0.002	0	0	0
OT36	0	0.001	0.001	0
OT37	0.001	0	0	0.001
OT38	0.001	0	0.001	0
OT39	0	0.001	0	0
OT40	0	0	0	0.001
OT41	0	0	0.001	0
OT42	0.001	0.001	0.001	0
OT43	0.001	0	0	0
OT44	0	0.001	0.001	0
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OT46	0	0	0.001	0
OT47	0	0	0.001	0
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OT56	0	0	0	0
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OT61	0	0	0	0
OT62	0	0	0	0
OT63	0	0	0	0
OT64	0	0	0	0
OT65	0	0	0	0
OT66	0	0	0	0
OT67	0	0	0	0

	NC	WT	PIVOT	SpRY
CXCR4-Target2	0.047	18.461	64.398	33.564
OT01	0.018	0.011	0.024	25.844
OT02	0.015	0.007	0.009	21.085
OT03	0.005	0.374	8.318	0.402
OT04	0.650	0.869	3.603	2.365
OT05	0.002	0.002	0.001	2.008
OT06	0.441	0.601	0.623	0.522
OT07	0.001	0	0	0.596
OT08	0	0.002	0.002	0.512
OT09	0.382	0.194	0.484	0.099
OT10	0	0	0.429	0.010
OT11	0.001	0.005	0.001	0.255
OT12	0.157	0.114	0.240	0.097
OT13	0.023	0.042	0.218	0.085
OT14	0.003	0.002	0.004	0.209
OT15	0	0.001	0.171	0.005
OT16	0.002	0.001	0.160	0
OT17	0.132	0.118	0.093	0.052
OT18	0.002	0.001	0.001	0.118
OT19	0	0	0.030	0.108
OT20	0.003	0.001	0.089	0.003
OT21	0	0	0.054	0.018
OT22	0.006	0.010	0.033	0.052
OT23	0.051	0.026	0.026	0.018
OT24	0.001	0	0	0.049
OT25	0.002	0.001	0.049	0.001
OT26	0.002	0.005	0.005	0.047
OT27	0.046	0.019	0.024	0.026
OT28	0.014	0.015	0.040	0.026
OT29	0.022	0.023	0.032	0.016
OT30	0.003	0	0	0.025
OT31	0.003	0.006	0.018	0
OT32	0.005	0.006	0.012	0.002
OT33	0	0.001	0.002	0.012
OT34	0.009	0.006	0.011	0.005
OT35	0.001	0.002	0.009	0.002
OT36	0.008	0.005	0.009	0.008
OT37	0.005	0.003	0.003	0.009
OT38	0.008	0.001	0.001	0.002
OT39	0.005	0.007	0.007	0.005
OT40	0.006	0.002	0.002	0.002
OT41	0.005	0.002	0.004	0.002
OT42	0.001	0.002	0.003	0.004
OT43	0.003	0.003	0.002	0.002

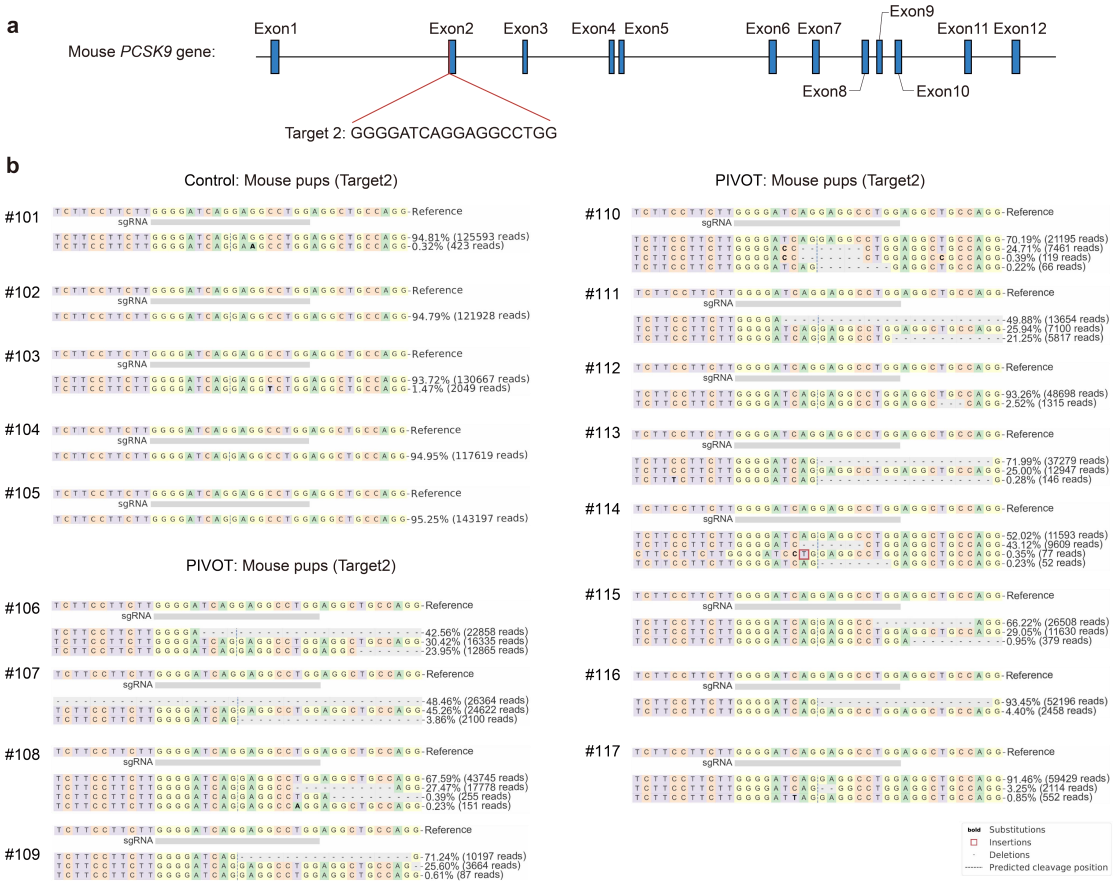
	NC	WT	PIVOT	SpRY
CXCR4-Target2	0.047	18.461	64.398	33.564
OT44	0.003	0.001	0.003	0.002
OT45	0.003	0.002	0.001	0.001
OT46	0	0	0.003	0
OT47	0.001	0.002	0.003	0.001
OT48	0.002	0.001	0.002	0
OT49	0.002	0.001	0.001	0
OT50	0	0	0.002	0.002
OT51	0.002	0	0.001	0.001
OT52	0.001	0	0.002	0
OT53	0	0.001	0	0.002
OT54	0.001	0.001	0.001	0.001
OT55	0.001	0.001	0.001	0
OT56	0	0.001	0	0
OT57	0	0.001	0.001	0.001
OT58	0.001	0.001	0.001	0.001
OT59	0	0.001	0.001	0
OT60	0	0.001	0.001	0
OT61	0	0	0.001	0
OT62	0	0	0.001	0
OT63	0.001	0	0	0
OT64	0	0	0.001	0
OT65	0	0.001	0	0
OT66	0.001	0	0	0
OT67	0.001	0	0	0
OT68	0.001	0	0	0
OT69	0.001	0	0.001	0
OT70	0	0	0.001	0
OT71	0.001	0	0	0
OT72	0	0.001	0.001	0
OT73	0	0.001	0	0
OT74	0	0.001	0	0
OT75	0	0.001	0	0
OT76	0	0	0	0
OT77	0	0	0	0
OT78	0	0	0	0
OT79	0	0	0	0
OT80	0	0	0	0
OT81	0	0	0	0
OT82	0	0	0	0
OT83	0	0	0	0
OT84	0	0	0	0
OT85	0	0	0	0
OT86	0	0	0	0

	NC	WT	PIVOT	SpRY
CXCR4-Target4	0.065	0.390	56.497	11.025
OT01	2.135	2.172	2.328	1.734
OT02	2.045	1.547	1.375	1.599
OT03	1.778	1.640	1.481	1.398
OT04	1.590	1.022	1.066	1.732
OT05	0.019	0.747	0.021	0.025
OT06	0.540	0.300	0.371	0.316
OT07	0.273	0.363	0.255	0.493
OT08	0.399	0.418	0.398	0.488
OT09	0.425	0.300	0.332	0.296
OT10	0.172	0.108	0.115	0.118
OT11	0.147	0.077	0.072	0.055
OT12	0.061	0.141	0.056	0.054
OT13	0.019	0.126	0.023	0.018
OT14	0.075	0.077	0.069	0.107
OT15	0.058	0.105	0.071	0.070
OT16	0.071	0.049	0.080	0.071
OT17	0.012	0.011	0.004	0.069
OT18	0.068	0.050	0.056	0.059
OT19	0.047	0.061	0.030	0.042
OT20	0.054	0.058	0.046	0.057
OT21	0.051	0.039	0.047	0.039
OT22	0.050	0.020	0.034	0.028
OT23	0.043	0.018	0.005	0.005
OT24	0.042	0.043	0.042	0.032
OT25	0.042	0.038	0.023	0.032
OT26	0.023	0.039	0.014	0.031
OT27	0.038	0.038	0.030	0.035
OT28	0.036	0.030	0.033	0.035
OT29	0.034	0.034	0.034	0.026
OT30	0.017	0.017	0.034	0.022
OT31	0.033	0.018	0.011	0.028
OT32	0.026	0.018	0.032	0.014
OT33	0.026	0.029	0.017	0.028
OT34	0.014	0.024	0.019	0.010
OT35	0.011	0.014	0.014	0.022
OT36	0.008	0.007	0.013	0.022
OT37	0.017	0.016	0.016	0.014
OT38	0.016	0.015	0.016	0.010
OT39	0.014	0.009	0.003	0.010
OT40	0.007	0.006	0.005	0.010
OT41	0.010	0.003	0.006	0.009
OT42	0.006	0.003	0.007	0.005
OT43	0.006	0.006	0.003	0.007
OT44	0.007	0.004	0.002	0.004
OT45	0.005	0.007	0.005	0.006
OT46	0.003	0.002	0.006	0.003
OT47	0.001	0.001	0.003	0
OT48	0.001	0.001	0	0.002
OT49	0.001	0	0	0.001
OT50	0.001	0	0	0
OT51	0	0	0.001	0
OT52	0	0	0	0

Supplementary Figure 6 | Evaluation of target-site compatibility of PIVOT with SpRY at endogenous loci. a, Overlapping target sequences of ParTasR and SpRY at four endogenous loci (*TTR*-target1, *TTR*-target4, *CXCR4*-target2, and *CXCR4*-target4) in HEK293T cells. ParTasR targets are in blue; red boxes mark regions of overlap with SpRY. **b,** On- and off-target analyses of WT-ParTasR, PIVOT, and SpRY at four genomic loci, with off-target sites containing 1–2 mismatches identified by Cas-OFFinder. Values are expressed as the mean of three independent biological replicates.



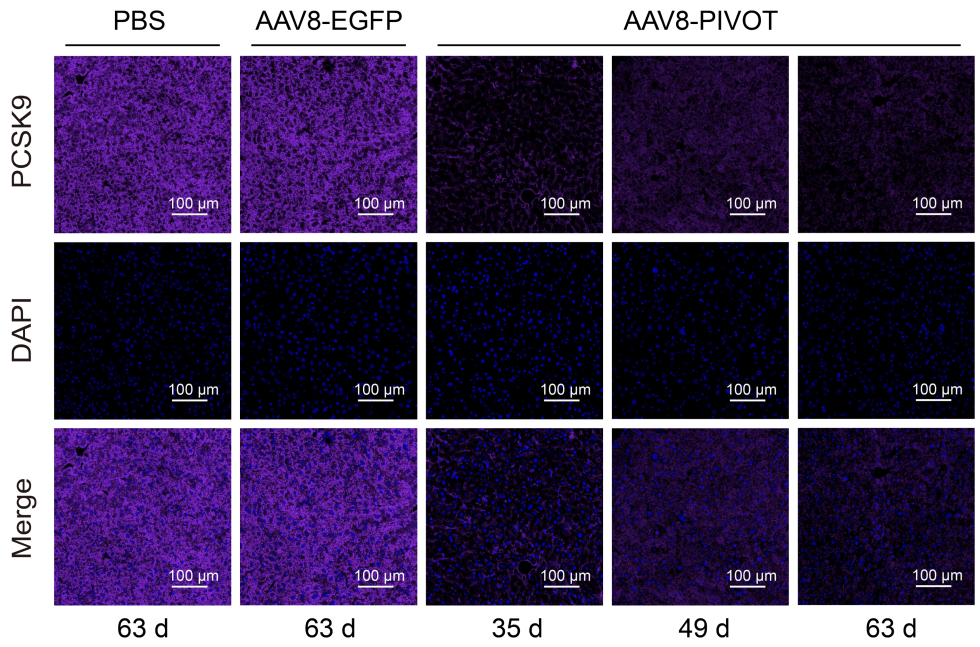
Supplementary Figure 7 | Selection of *PCSK9* target sites and assessment of embryonic development. a, Editing efficiencies of plasmid-delivered PIVOT at endogenous *PCSK9* target sites in mouse N2a cells. Indel frequencies were quantified by targeted amplicon sequencing. Values and error bars are expressed as mean ± s.e.m. (n = 3 independent biological replicates). **b,** Blastocyst development rates of untreated embryos and embryos injected with ParTasR-p3.5 mRNA and *PCSK9*-target2-targeting tigRNA-r3.13. Values and error bars are expressed as mean ± s.e.m. (n = 3 independent microinjection batches).



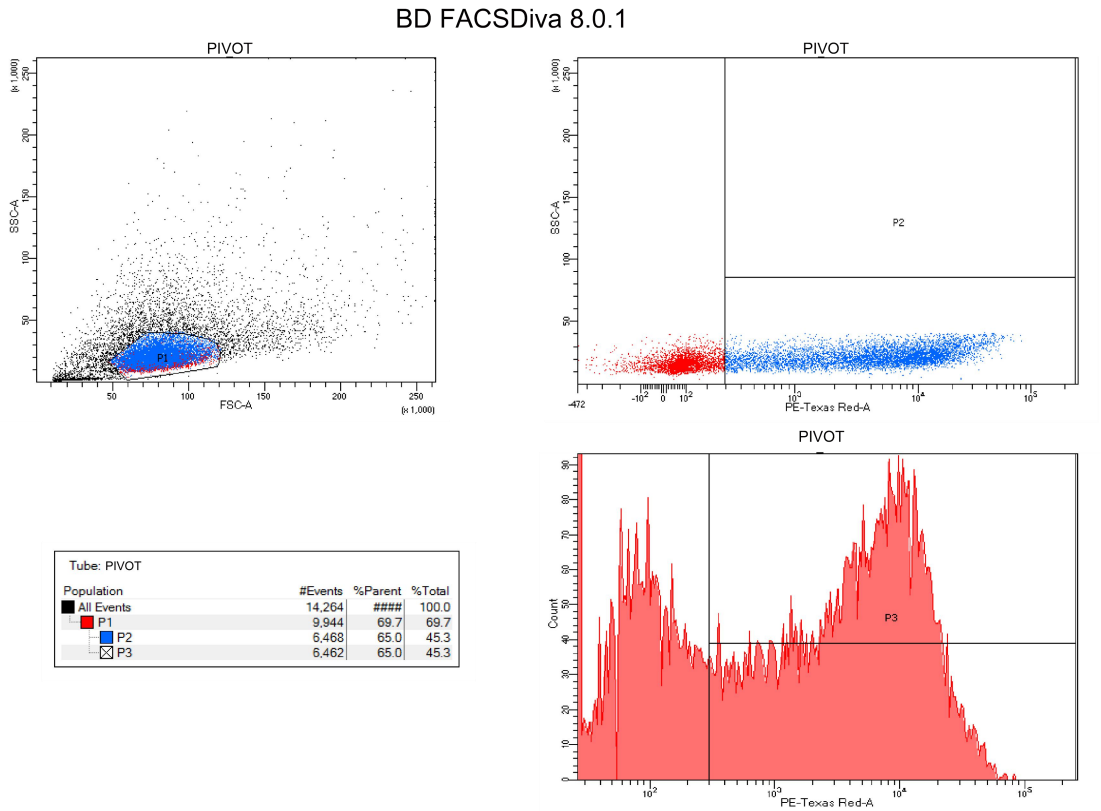
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	Gene	No. of injected embryos	No. of two-cell-stage transferred embryos (%)	No. of offspring (%)	Gene editing efficiency in the offspring (%)
PIVOT	*PCSK9* Target2	48	43 (89.6)	12 (27.9)	50.97

Supplementary Figure 8 | Editing efficiency of PIVOT at the PCSK9 locus in mice. a, Schematic diagram illustrating PIVOT targeting of target 2 in the mouse *PCSK9* gene. **b,** Distribution of mutant alleles among twelve PIVOT-mediated gene-edited mice and five control mice at the *PCSK9* locus. **c,** Summary of injection parameters for generating *PCSK9*-knockout (KO) mice through PIVOT-mediated editing of the mouse *PCSK9* gene.



Supplementary Figure 9 | Hepatic PCSK9 expression after AAV8-mediated PIVOT delivery. Representative immunofluorescence images of PCSK9 expression in liver sections at days 35, 49, and 63 after the indicated treatments. PCSK9 and nuclear staining are shown as indicated. Scale bar: 100 μm.



Supplementary Figure 10 | FACS gating examples for mCherry-positive cell sorting conditions.

Supplementary Table 1 Detailed sequence information of ParTasR variant.

Mutation	Protein sequence (proteins different from the wild-type sequence are indicated in red font)
ParTasR_wild-type	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W (p1.1)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F (p1.2)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSDT HLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_L256R (p1.3)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_D276Q (p1.4)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_S280R (p1.5)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ Q239F (p2.1)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ L256R (p2.2)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS

ParTasR_E217W+ D276Q (p2.3)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ S280R (p2.4)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+L 256R (p2.5)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSDT HLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+ D276Q (p2.6)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQT HLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+S 280R (p2.7)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSDT HLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_L256R+ D276Q (p2.8)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_L256R+S 280R (p2.9)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_D276Q+ S280R (p2.10)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ Q239F+L256R (p3.1)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD

	THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ Q239F+D276Q (p3.2)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ Q239F+S280R (p3.3)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ L256R+D276Q (p3.4)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ L256R+S280R (p3.5)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+ D276Q+S280R (p3.6)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+L 256R+D276Q (p3.7)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQT HLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+L 256R+S280R (p3.8)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSDT HLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+ D276Q+S280R (p3.9)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQT HLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS

ParTasR_L256R+D276Q+S280R (p3.10)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+Q239F+L256R+D276Q (p4.1)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLSLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+Q239F+L256R+S280R (p4.2)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSD THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+Q239F+D276Q+S280R (p4.3)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQLEIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+L256R+D276Q+S280R (p4.4)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKQRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_Q239F+L256R+D276Q+S280R (p4.5)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEEVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQT HLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS
ParTasR_E217W+Q239F+L256R+D276Q+S280R (p5.1)	MRQVAIDWAFAEEKLAVYDGKKVLKAVPKLKAGDEIFAENIPMKHAAQWLKDGIIIRRCRPNDTAALR KEIGQEKTDALDAKLIWQLAEAHPEKFREWKGDPQLTTLYRAFKEVQRCRVGQSNRVWAKGEETATAV LDDLEKTERKIVKAIEKELKSYKVWDWLSQIKGIGVATGGGLVGLIAKYGIENIRQVSSLWHLFGLHVVE GKAPRRTKGEWVSYVPEAKTLVLGVIADCFIKFRSPVYRDIYDQEKARQREIEYPEGELASKFLGYKKSQ THLRLNHAHRRAIRKMMKIFVQHVWLAWRTCEGLETRPLYCHEYLGHEHFIEPPVKIQPEGS

Supplementary Table 2 Detailed sequence information of engineered tigRNAs.

tigRNA variants	RNA sequence (regions different from the wildtype tigRNA sequence are indicated in red font; the spacer is indicated in blue font).
tigRNA wild-type scaffold	AGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCG
tigRNA r1.1 scaffold	AGCCANNNNNNNNNUGUCAAACCANNNNNNNNNUGCG
tigRNA r1.2 scaffold	AGCCANNNNNNNNNUGAAUAUACCANNNNNNNNNUGCG
tigRNA r1.3 scaffold	AGCCANNNNNNNNNUGAUAUUGCCANNNNNNNNNUGCG
tigRNA r1.4 scaffold	AGCCANNNNNNNNNUGUCAUGUCCANNNNNNNNNUGCG
tigRNA r2.1 scaffold	AGACCNNNNNNNNNGUAAACACCNNNNNNNNNGUCG
tigRNA r2.2 scaffold	AGUAUNNNNNNNNNAUAAACUAUNNNNNNNNNAUCG
tigRNA r2.3 scaffold	AGUACNNNNNNNNNAAAAACUACNNNNNNNNNAACG
tigRNA r2.4 scaffold	AGCUUNNNNNNNNNGCAAACCUUNNNNNNNNNGCCG
tigRNA r3.1 scaffold	GGGAGGGGCGGGUCUGGGGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGC
tigRNA r3.2 scaffold	ACAUGAGGAUUACCCAUGUGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGC
tigRNA r3.3 scaffold	GGCCGUCGACGGCCGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGC
tigRNA r3.4 scaffold	GCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGGGAGGGAGGGAGAGGG
tigRNA r3.5 scaffold	GCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGGGAGGGGCGGGUCUGGG
tigRNA r3.6 scaffold	GCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCACAUGAGGAUUACCCAUGU
tigRNA r3.7 scaffold	GGGAGGGAGGGAGAGGGGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCACAUGAGGAUUACCCAUGU
tigRNA r3.8 scaffold	GGGUGGGCCUGGGAGGGGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGGGUGGGCCUGGGAGGG
tigRNA r3.9 scaffold	GAAACACCGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGAAACACC
tigRNA r3.10 scaffold	GAAACACCGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGCCCUGAAGAGGGC
tigRNA r3.11 scaffold	GAAACACCGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCGCCGUGUUCGGC
tigRNA r3.12 scaffold	AGUGUGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCACACU
tigRNA r3.13 scaffold	GAUGUGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCACAUC
tigRNA Mobius_V1 scaffold	CCANNNNNNNNNUGAAACCCANNNNNNNNNUGAAAC
tigRNA Mobius_V2 scaffold	AGCCANNNNNNNNNUGAAACCCANNNNNNNNNUGCG

Supplementary Table 3 Target genomic sites, guide sequences, and primer sequences used in this study.

Target	ParTasR_guide sequence	SpRY_guide sequence	NGS-Primer-F (5'-3')	NGS-Primer-R (5'-3')
B2M_Target 1	TCAACTTCAATGTCGGAT	AGTCAACTTCAATGTCGGAT	CCCAAGTGAAATACCCTGGCA	TCATCTTTTTCAGTGGGGGTGA
B2M_Target 2	GATGAAACCCAGACACAT	TGGATGAAACCCAGACACAT	CCCAAGTGAAATACCCTGGCA	TCATCTTTTTCAGTGGGGGTGA
B2M_Target 3	GATGAAACCCAGACACAT	AGAAAGACCAGTCCTTGCTG	TCCAGCAGAGAATGGAAAGTCA	TTCAGCAGCTTACAAAAGAATGT
B2M_Target 4	ATGAGTATGCCTGCCGTG	AGATGAGTATGCCTGCCGTG	TCCAGCAGAGAATGGAAAGTCA	TTCAGCAGCTTACAAAAGAATGT
VEGFA_Target 1	AGGAGGGCAGAATCATCA	GGAGGAGGGCAGAATCATCA	GAAGTGAGGAGGGAGGAGGG	TGATCCTTATATTCCTGTGCCCC
VEGFA_Target 2	TCCAGGCCCTCGTCATTG	ACTCCAGGCCCTCGTCATTG	GACCCTGGTGGACATCTTCC	CAACTCAGGGGCAGGAGC
VEGFA_Target 3	GTGGGCACACACTCCAGG	CAGTGGGCACACACTCCAGG	GACCCTGGTGGACATCTTCC	CAACTCAGGGGCAGGAGC
VEGFA_Target 4	AGGAGTCCAACATCACCA	TGAGGAGTCCAACATCACCA	GACCCTGGTGGACATCTTCC	CAACTCAGGGGCAGGAGC
CXCR4_Target 1	AATGTACAAACGTTTGAA	TAAATGTACAAACGTTTGAA	GTAGCAAAGTGACGCCGAGG	GAGTACGGGTACCTCCAATGT
CXCR4_Target 2	ACCGCATCTGGAGAACCA	CCACCGCATCTGGAGAACCA	GCCGCGGCCAGAAACTTCA	AAAACTCCTTTCGGTGACCCTTTTT
CXCR4_Target 3	CTGAGTGCTCCAGTAGCC	GCCTGAGTGCTCCAGTAGCC	GCCGCGGCCAGAAACTTCA	AAAACTCCTTTCGGTGACCCTTTTT
CXCR4_Target 4	GTCACCGAAAGGAGTTTT	GGGTCACCGAAAGGAGTTTT	TCCAGTTTCAACCTGCTTTGTCATA	TCTCCTCGACTCACAGAGAAAAAGA
CXCR4_Target 5	GTGTCTCCCCCTTGAGTC	ATGTGTCTCCCCCTTGAGTC	CATGCCTATATAGTGCGGGTGG	CAGACAATGTAACTCGCTCCAAGAC
BCL11A_Target 1	CTGGTGTGTTATGTCTAA	CCCTGGTGTGTTATGTCTAA	GATACAGGGCTGGCTCTATGC	CAAACGGCCACCGATGGAGA
BCL11A_Target 2	CAACTGTTAGCTTGCACT	AGCAACTGTTAGCTTGCACT	AGAGCAGATAGCTGATTCCAGTG	TCACCAAGAGAGCCTTCCGA
BCL11A_Target 3	AAGCTAGTCTAGTGCAAG	TGAAGCTAGTCTAGTGCAAG	AGAGCAGATAGCTGATTCCAGTG	TCACCAAGAGAGCCTTCCGA
BCL11A_Target 4	AACTGTTAGCTTGCACTA	GCAACTGTTAGCTTGCACTA	AGAGCAGATAGCTGATTCCAGTG	TCACCAAGAGAGCCTTCCGA
TTR_Target 1	GTTCTAGATGCTGTCCGA	AAGTTCTAGATGCTGTCCGA	GTTCCTGATAATGGGATCAGTGT	GGAGGGTTCTTTGGCAACTTAC
TTR_Target 2	GAACTTTGACCATCAGAG	TAGAACTTTGACCATCAGAG	GTTCCTGATAATGGGATCAGTGT	GGAGGGTTCTTTGGCAACTTAC
TTR_Target 3	TGGTCAAAGTTCTAGATG	GATGGTCAAAGTTCTAGATG	GTTCCTGATAATGGGATCAGTGT	GGAGGGTTCTTTGGCAACTTAC
TTR_Target 4	GAACACATGCACGGCCAC	CTGAACACATGCACGGCCAC	ATCCTTTCACTCTGATCAATTTTGT	GCAGATGATGTGAGCCTCTCT
SOCS1_Target 1	TGCGAACGGAATGTGCGG	CGTGCGAACGGAATGTGCGG	GACAATGCAGTCTCCACAGC	GACAATGCAGTCTCCACAGC
SOCS1_Target 2	GAAAAAGCAGTTCCGCTG	GCGAAAAAGCAGTTCCGCTG	CCGATTACCGGCGCATCA	CGAAGAGGCAGTCGAAGCTC
SOCS1_Target 3	TGTCGCGCACCAGGAAGG	GCTGTCGCGCACCAGGAAGG	CCGATTACCGGCGCATCA	CGAAGAGGCAGTCGAAGCTC

Supplementary Table 4 Sequences of primers used to amplify nuclease-dependent off-target sites.

Target	guide sequence	Mismatches	NGS-Primer-F (5'-3')	NGS-Primer-R (5'-3')
CXCR4-Target2 OT01	ACCGCATCcaGAGAACCA	2	GAACATGTAGGGAGCCAGGC	ACCTTGGCCCACACATACTG
CXCR4-Target2 OT02	ACCGCATCcaGAGAACCA	2	AGCACTTCACCGTCTGAGAG	TGCCTGACGTGGGGATTTAG
CXCR4-Target2 OT03	ACCaCATCTGGAGAACCA	1	CAAAGGGCTTTGCAGACACC	CAGAGACAGAGTGGACGCTG
CXCR4-Target2 OT04	ACCGtATgTGGAGAACCA	2	ACCACTTGTGAGAGGCAAGG	TCTTTCGTTGCAGGTCAGCC
CXCR4-Target2 OT05	ACCaCATCTGGAGAACCc	2	GATCCACCCATCTCGGCTTC	CGAATTACGTGAGCGCAGAG
CXCR4-Target2 OT06	ACCaCATCTGGgGAACCA	2	ACAGAGCAAGAGTCCCAAGC	TCTGGGGTCTGAGATCTGGG
CXCR4-Target2 OT07	ACCatATCTGGAGAACCA	2	CCCTGCTCATGAGAGACAAGG	ACAGGTCAGCCACTTGCATG
CXCR4-Target2 OT08	ACCaCATgTGGAGAACCA	2	ACTCATGACAGGCAAGGAGC	ACCTTTCGTTGCAGGTCAGC
CXCR4-Target2 OT09	ACCaCATgTGGAGAACCA	2	ACCACTGAACTTAGGAGCAACC	GTGTTTCTGGAGTTGGCTGC
CXCR4-Target2 OT10	ACCaCATCTtGAGAACCA	2	ACACACGACTGCTTGTTTGC	AGTACTGCTGGTCTGGTTGG
CXCR4-Target2 OT11	ACCaCATgTGGAGAACCA	2	CTCCTGACCTCGTGATCTGC	GACATGAACTGTTCGGAGGC
CXCR4-Target2 OT12	ACCaCATgTGGAGAACCA	2	GCTCATGAGAGGCAAGGAGG	GCAGGTCAGCCGCTTACATG
CXCR4-Target2 OT13	ACCaCATgTGGAGAACCA	2	AGGCAAGGAGTTCAGTGAGC	TCATTGCAGGTCAGCCACTC
CXCR4-Target2 OT14	ACCaCATtTGGAGAACCA	2	TGGTTGCCTGAAGTGGAGTC	TGCTTCCCCTTTGCCTTCTG
CXCR4-Target2 OT15	ACCaCATCTGGAGAAtCA	2	CCTAGGGGATGCTGATGCTG	ACAGTTCCTACCACCTGCTC
CXCR4-Target2 OT16	ACCaCATCTGGAGAAtCA	2	TTTCTCACAGGTTCCTGGGC	TGTCTTCCACGAAACCGGTC
CXCR4-Target2 OT17	ACCGtATgTGGAGAACCA	2	TGGTTTTGGGGTTTCTGGTG	AGGAGCAACCAACCAGCTTC
CXCR4-Target2 OT18	ACCtCATCTGaAGAACCA	2	TGGGTATTTGTGGGTGCCTC	TCATGCCACTGTACTCCAGC
CXCR4-Target2 OT19	ACCGCATtTtGAGAACCA	2	AGAGACGGGGTTTCACTGTG	CACTAAGAAAATTAACAGCCAAAGC
CXCR4-Target2 OT20	ACCatATCTGGAGAACCA	2	ACCTAGGAGGGACCAACCAG	GGGGTTTCTGGAGTTGGCTG
CXCR4-Target2 OT21	ACCGCAcCTGGAGAACCA	1	TGATATTGATGGTGGTCTGGGG	TGCTGGGATTACAGGCTTGAG
CXCR4-Target2 OT22	ACCGCAcCTGGAcAACCA	2	GGACATTCTCTAAAGAAAGATGGAC	GATTCTCCTGCCTCAGCCTC
CXCR4-Target2 OT23	ACCGCAgCTGGAGAcCCA	2	CCTGTTCTCTTGGGAGTGCC	TGCCAGTAACAGGGAGAAGC
CXCR4-Target2 OT24	ACCaCATtTGGAGAACCA	2	CCAGTAGGTTTGAGATGGGGC	AAAGTGCTTGAGGCTGGGAG
CXCR4-Target2 OT25	ACCGCATCTGGAagACCA	2	GGCCAATTCCAAACCTGTTCC	TTTTCCTGGCTGGCAGAGAG
CXCR4-Target2 OT26	ACaGCATCTGGAGAACCt	2	AGACCCCATTTTCTCCCTGC	CATCACCATGCCCGACTAAAC
CXCR4-Target2 OT27	ACCaCATgTGGAGAACCA	2	TCCACTGAACTTAGGAGCAACC	GGGTTTCTGCAGTTGGTTGC
CXCR4-Target2 OT28	ACCGtATgTGGAGAACCA	2	CTTAGGAGCAAACAACCAGCG	TTTTGGCATTTCTGGAGTTGGC
CXCR4-Target2 OT29	ACCGCcTCaGGAGAACCA	2	GTCATGCATAGCACAAGCCC	TGCCTGGAATAGTTCTGAGGTG
CXCR4-Target2 OT30	ACCcCATgTGGAGAACCA	2	GGGGCTGTCCTGAGCATTG	CTAGTTGTGGGTGGAGCTGG
CXCR4-Target2 OT31	ACCcCATCTGGAaAACCA	2	TCACTGGAAACCTGCTGTGG	TGCAGAAGACAGCAGGACAG
CXCR4-Target2 OT32	ACCaCATgTGGAGAACCA	2	CACTGCTCATGAGAGGCAGG	GTCACTCGCATGGTAAGAGC
CXCR4-Target2 OT33	ACCaCATgTGGAGAACCA	2	GGTTTTGAAGTTTCTGGAGTAGGC	AGGAGCAACCAACCAGCTTC
CXCR4-Target2 OT34	ACCGCAgCTGcAGAACCA	2	GCACTGACTTGGCCTGAAAC	CAACTGGAGTCTGTGGCTGG
CXCR4-Target2 OT35	ACaGgATCTGGAGAACCA	2	TTCATGGGGACGGGAACAAG	ACAGACGCAGCCTCTCTTTC

CXCR4-Target2 OT36	ACCtCcTCTGGAGAACCA	2	TTGGCCAGAAGAGCTCATGG	ATTACGGGTCAGGCACTTGG
CXCR4-Target2 OT37	ACCaCATgTGGAGAACCA	2	GGGGTTTCTGGAATTAGCTGC	TGTCCACTGAACCTAGGAGC
CXCR4-Target2 OT38	ACCGCATCTGGgGgACCA	2	GCAGGAAGGATGTGACCCTC	GGCTGAGGTGGGAGAATCAC
CXCR4-Target2 OT39	tCCGCATCTGGAGAAgCA	2	CTGCAGTGAGCCATGATTGC	TCCTCCTTGGTCAGCAAGTG
CXCR4-Target2 OT40	ACCaCATtTGGAGAACCA	2	TCTCACTGGTGATGCTGCTG	TAAACCATGCCCCACCTTCC
CXCR4-Target2 OT41	ACCtCcTCTGGAGAACCA	2	AGCACACACAAACGCACAAC	GCCCCTTAGCAATCCTGAGG
CXCR4-Target2 OT42	ACtGCATCTGGAGAAgCA	2	TGGCCTCCTGAGACTTTTCC	TCCAAGACCAAGATGCCAGC
CXCR4-Target2 OT43	ACCaCAcCTGGAGAACCA	2	GAGAGCCGGTTAGCACTGTC	TTAGTGGCATGTTGGGGCTG
CXCR4-Target2 OT44	ACaGCAaCTGGAGAACCA	2	CCACTCCAGTTTGCCAAAGG	GCCCAAAAGTGTCTCACATGG
CXCR4-Target2 OT45	ACCaCATgTGGAGAACCA	2	AGGAGCAACCAACCAGCTTC	TGAAGCTATGCAACCCCACC
CXCR4-Target2 OT46	ACCaCATgTGGAGAACCA	2	GCATTTCTGGAGTTGGCTGC	TCCAGTGAACTTAGAGCAGCC
CXCR4-Target2 OT47	ACCGtATgTGGAGAACCA	2	AGTATGTGCTTCTGGAACTGGG	TGGAGAACACTGACAGTTCCTG
CXCR4-Target2 OT48	ACgcCATCTGGAGAACCA	2	TCAGAGCAGTGTCCAGCATG	TGCAGAAAAGCACCAGGTTG
CXCR4-Target2 OT49	ACtGCATCTGGAGAtCCA	2	AGGGCCCTCAGCAAAGAATG	GCTGGAGCTTGTACTAGGGC
CXCR4-Target2 OT50	cCCGCATCTGGAGAAaCA	2	CTCAAGGCAGGAGGGAACAG	TGGGCTGGTTTCCTTACCAC
CXCR4-Target2 OT51	ACCaCATCTGGAGAACtA	2	GTCCTTCACACACACTTCAGAC	AGCAGATGTCACCTCTTGGC
CXCR4-Target2 OT52	ACCtCATCTGtAGAACCA	2	TGGCCTGTATCTGCAGTCAG	CTGTCCTCTCACCAGCACAC
CXCR4-Target2 OT53	ACCGtATgTGGAGAACCA	2	TATTGCAGGTCAGCCACTCG	GGCCAGGAGGTTAGTGACTC
CXCR4-Target2 OT54	ACCGCtTCTGGAGAAgCA	2	AAACCCCATCTGCTTCCCAG	CATGGTTTCCTGTCCTCCCC
CXCR4-Target2 OT55	ACCGgAgCTGGAGAACCA	2	GAGGACGACAGTGGGGAAAG	CCCAGAGGGCTTCCTTCAAG
CXCR4-Target2 OT56	ACCGCATCTGGAacACCA	2	CCAACCTGGATCACTCACCC	GGAGAGTTGGGTCCTGATCC
CXCR4-Target2 OT57	AgCGCATCTGGAGcACCA	2	ACCAGAGCAAACCACAGACC	GGTTTGCAGCACGTCATACC
CXCR4-Target2 OT58	ACCGCATgTGGAGAAgCA	2	GCAGATTCCAATTCCAGCGG	GCCAGGTAAAGGGAGTGGAG
CXCR4-Target2 OT59	tCCGCATCTGGAGcACCA	2	AAACCTGAGGCTCCGTCTTG	AGGTTTGGCTTCCCCATCTC
CXCR4-Target2 OT60	ACCaCATgTGGAGAACCA	2	TCCGATGAACTTAGGAGCAACC	GAGCTTCTGGAATTGGCTGC
CXCR4-Target2 OT61	ACaGCATCTGGAGAAaCA	2	AAGCCTCTTCAGAAGCCAGC	ACAGTGCTGGGATTACAGGC
CXCR4-Target2 OT62	ACCaCATCTGGAGAACaA	2	TCTGTAACAGTAGATCTAGGTACCC	CCTACACCAGAGCAGCAGAG
CXCR4-Target2 OT63	ACCaCAcCTGGAGAACCA	2	GTTTTGATGGTGGCAGCTGG	GATCCTCCTGCCTTGGACTC
CXCR4-Target2 OT64	ACgGCATgTGGAGAACCA	2	CTCACAGAGTTTGCAGTGGC	ACCAAAAGGCTTGCTTGATGC
CXCR4-Target2 OT65	ACCaCATtTGGAGAACCA	2	GAAGTGGTGCAGGTGCTTTG	ACCACTGTAAAGGGCTCTGC
CXCR4-Target2 OT66	ACCaCATtTGGAGAACCA	2	CATGCTGGAACGCAAGAGC	TGGGCCTCCTAGGGAATCTC
CXCR4-Target2 OT67	ACCaCATtTGGAGAACCA	2	TGGGCCTCCTAGGGAATCTC	CATGCTGGAACGCAAGAGC
CXCR4-Target2 OT68	ACaGCATCTGGAGAAtCA	2	GAGCTCCCTTCTCAACTGGC	GCCAATAGGAGACCCAGCAG
CXCR4-Target2 OT69	ACtGCAcCTGGAGAACCA	2	ATGAAAGCCCTTGGAGCAGG	GTGCCTCCCTTGTTGCAAAG
CXCR4-Target2 OT70	ACacCATCTGGAGAACCA	2	GACACTGGTGGGATCTCGAC	ATGGATGGCACCACAGTTCC
CXCR4-Target2 OT71	AaCGCATCTGGAGAAgCA	2	CCAGGGAGATCAAGTGGCTC	CGTGGACAGTCTTTGAAGCC
CXCR4-Target2 OT72	ACCcCATCTGGAGtACCA	2	AGAGGATGGGTGTGCACATG	CAGGCCGTGGAGTAATCCTC
CXCR4-Target2 OT73	ACCaaATCTGGAGAACCA	2	TCTCGGTGATTTGACAGGGG	GCCAGTCCAGTCTAAGGAGC
CXCR4-Target2 OT74	gCtGCATCTGGAGAACCA	2	TGTGACACATGGGACTGGTG	CTCAAAGCCCCTCCCAGATG
CXCR4-Target2 OT75	ACCGCATtTGGAGAAgCA	2	AGCCACAGCCCTTGTCTAAC	TGACAAGTTCCCAGGTGGTG
CXCR4-Target2 OT76	ACtGCATgTGGAGAACCA	2	AATCGCTTGAACCCAGGAGG	TCGTGAGAGGCGAGGAATTC
CXCR4-Target2 OT77	gCCGCAcCTGGAGAACCA	2	TTTGCCCTTCCAGAGCTCAC	GGGCCCCTGATAGAATTGGG

CXCR4-Target2 OT78	AtCaCATCTGGAGAACCA	2	ACCAGTCAAATGGCAGGGAG	CAGAAGAGGCAAGGGTAGGG
CXCR4-Target2 OT79	ACCaCATCTtGAGAACCA	2	CTGACGCATAGCAGGCATTC	CCACGGTCCTGGCATAGTG
CXCR4-Target2 OT80	ACCcCATCTGGAaAACCA	2	GCAGCAATGACAGGGATAGC	GTCCAGGGAGATTGAGCAGG
CXCR4-Target2 OT81	ACaGCATCTGGAGgACCA	2	GGAAGACTGAGGCAGGAAGG	CTGGACATTCAGGAAGGCCC
CXCR4-Target2 OT82	ACCGCAcCTGGAGAAaCA	2	ATTCTGATGCAGGCGGTGAG	CTAGTTCTGCCCTCTGGAGC
CXCR4-Target2 OT83	AaCaCATCTGGAGAACCA	2	AACTCTGTGTCTCTGCACCG	TACAGGTGTAAGCCACTGCG
CXCR4-Target2 OT84	ACaGCAaCTGGAGAACCA	2	GCCTGGATCCAAGAAAACGC	TCTCAGAGATTGACAAATGCTACG
CXCR4-Target2 OT85	ACCtCAcCTGGAGAACCA	2	GAGTTGGCTGAGCTGCAATC	TGGTTTCTGATTCTGTAGGTCTGG
CXCR4-Target2 OT86	ACCGCATCTGGAcAACgA	2	CAACAGCAAGCAGGTGGTTG	ATCAGAAACACAGCTGGGGC
CXCR4-Target4 OT01	aTCACCGAAtGGAGTTTT	2	GGTCACCCTGACTCACTGTG	TCTCAAGCAACGTTTTGACTGG
CXCR4-Target4 OT02	GTCtCCGAAAGGcGTTTT	2	AACTGAAGTGGCTAGGACGC	AATCAGGAGGCTGAAGCAGG
CXCR4-Target4 OT03	GTCACtGAAAGGAtTTTT	2	AGCAAAGGCAGGAGGAGAAC	ATATTCACCGAGTGGGAGGC
CXCR4-Target4 OT04	GTCACaGAAAGGAaTTTT	2	TCACCACATCAAAGCCCTCC	AGGACGTCTTGTTCTCACCG
CXCR4-Target4 OT05	GTCACCaAAAGGAGTTTT	1	ATCCCTGGAGAAGGTGTGTG	CTTCCACCTCAACTCCTGGC
CXCR4-Target4 OT06	GTCACCGtAAGGAGcTTT	2	CCTACAGCTGTACTAGACCCAC	TAGCTGGGATTACAGGCACC
CXCR4-Target4 OT07	GTCACtGAAAGtAGTTTT	2	CCTTGCACTTCTCCTTCTTGC	ACAGGGACCCAGTTGTAACC
CXCR4-Target4 OT08	GTCACCaAAAGGAcTTTT	2	CCTTTCTTTTGTTTCAGCAGGTTG	CCCCATAGGCCTCAAAGCTC
CXCR4-Target4 OT09	GaCACCaAAAGGAGTTTT	2	TTCTTCATCCTCTATGGCTCTACGG	ATTCTTACTGGACTCTATGGAAGTT
CXCR4-Target4 OT10	GTCACtGAAAGtAGTTTT	2	GTTTCACCATGTTGGCCAGG	ACACAGCTGAATGCAAAGGC
CXCR4-Target4 OT11	GTCACCtAAAGGAGTTTT	1	CACATCAAAATCCTGGTGCATG	ATGCTTAAGCTGTGCCAAGC
CXCR4-Target4 OT12	GTCACCtAAAGGtGTTTT	2	GGTCTCATCTGCTCTTGGTAGC	GCATTTTCAATCCTTGACTACTGC
CXCR4-Target4 OT13	GTCAgCGAAtGGAGTTTT	2	ACTGTTCTGCTGAGTTGCCC	GAAAGGGAGAAGGGAGGGTG
CXCR4-Target4 OT14	GcCACCaAAAGGAGTTTT	2	ATGGTGGTTTCAAAGCTAGAGAG	ACCATGCTTACTACCCAGGTG
CXCR4-Target4 OT15	GTCtCCaAAAGGAGTTTT	2	ATTCTGCTGCTCCTGGACAC	TCCCCAGCAAGGTTGTCATG
CXCR4-Target4 OT16	GTCAgCtAAAGGAGTTTT	2	AGGATTCACATCTGGGCAGC	AAAGTGCTGGGGTTACAGGC
CXCR4-Target4 OT17	GTCACaGgAAGGAGTTTT	2	CCTCTTGGGAAGGACAGGAC	CGCCTGAGACCCAGTTACTC
CXCR4-Target4 OT18	GTCACCGAAgGGAGTTTT	1	TGCTGGGCTGAGATGGAAAG	TCTGGGAGAGGGATCATGGG
CXCR4-Target4 OT19	GTCACaGtAAGGAGTTTT	2	GGTGGTTTCCCCAGAGAAGG	GCTGGTCTCGAACTCCTGAC
CXCR4-Target4 OT20	GTCACCtAAAGGAcTTTT	2	GTCTTGCTGCTATTGCTCCG	TGGTTCTAAGTCCTGGAGGC
CXCR4-Target4 OT21	GaCACaGAAAGGAGTTTT	2	CAGAAGGAGATTGCAGTGGC	TGGATAACAGAGTGAGAGCCTG
CXCR4-Target4 OT22	GTCACCGAAAGGtcTTTT	2	TAGCTGCACCAGGAAAAGGG	AGCAATGCCTCTTCTCTTGC
CXCR4-Target4 OT23	GTCACCGAAAGcAGTTTc	2	TGCTGTGCAGAAGCTCTTTAG	GCAGTGAGCTGAGATTGTGC
CXCR4-Target4 OT24	GTCACCaAAAGGAtTTTT	2	TCTCTCCACCTCCTAAGCCC	ATCGGAGTGAAAGGCCACAG
CXCR4-Target4 OT25	tTCACCGAAAGcAGTTTT	2	CTAGGCCATAGCTCCACGC	TGAACACGCACTTGGAAATGC
CXCR4-Target4 OT26	GaCACgGAAAGGAGTTTT	2	TAGGGACCAAGGAGTCATGG	CATCTACATCAGGGCCTGGG
CXCR4-Target4 OT27	GTCACCGAgAGGAGTTTT	1	GCCACTCAGAGGAGACACAC	CTGGGCCAGCTTGTTTTCAG
CXCR4-Target4 OT28	GTCACCtAAAGcAGTTTT	2	CTTGGTTGCCTGCTCTATGC	ATGTCCTTCAGCCCCAATCC

CXCR4-Target4 OT29	GTCAggGAAAGGAGTTTT	2	TGATTGCTCTAGCCTGGGTG	CCTGCCATTCTCCCAAAAGC
CXCR4-Target4 OT30	GTCACCGAAtGcAGTTTT	2	GCACAGAAGCCTTCAACTACAG	ACAACCCAGGCTTTCCCTAC
CXCR4-Target4 OT31	GTCACtGgAAGGAGTTTT	2	AAGTGCTGGGATTACAGGCG	TGCACATATCACTCCTGGGC
CXCR4-Target4 OT32	GTCACaGAAAGGtGTTTT	2	GGGAATGGATTGGGGAAGGG	GAAGGTTTGCTGACGGCTTG
CXCR4-Target4 OT33	GTCtCtGAAAGGAGTTTT	2	TGTCTGGCAAATGTGAACTGG	TAACCCAAGGTGGTGGTGTG
CXCR4-Target4 OT34	GTCAagGAAAGGAGTTTT	2	ACTCAAGGCCCCACAATCAG	GTTCACGGCAGAACTAAGGG
CXCR4-Target4 OT35	aTCACaGAAAGGAGTTTT	2	GACCTGTCTCTGCCTCAACC	GTGCTGCCTGTCCCAAATTG
CXCR4-Target4 OT36	GTCACCGAAAaaAGTTTT	2	GCCAGAGACTACGTGCTTTG	TGCTGGCCCACATCAGTATC
CXCR4-Target4 OT37	tTCACCaAAAGGAGTTTT	2	TCTCCAATGATGACTTCCACCTC	AGGAGGTGTGTGCTGACTTG
CXCR4-Target4 OT38	GgCACaGAAAGGAGTTTT	2	CACAGCCAAGGGAATTGAGG	GGCTCCTTCCAGAGTCTTTGG
CXCR4-Target4 OT39	GTCACCaAAAGGAGTTcT	2	GGATCATCCTGACTGCTCCC	AGCCTGCATTGGAAACATCC
CXCR4-Target4 OT40	GTCACCtAAAGaAGTTTT	2	ACCCCTTTAATAAGAGAAACTCCTC	TCCAGCACTCTAGGTTACATACG
CXCR4-Target4 OT41	GTCACaGAAAGtAGTTTT	2	ACTGGGCTGAAACTCTGGAG	TCATCAAGGAAGGAGGCATCTC
CXCR4-Target4 OT42	GTCAgCGAAAGGAaTTTT	2	GCTCAGTTTTGCACAGGGTG	TGGTTTTACACAGCAACTGGG
CXCR4-Target4 OT43	GTCACCcAAAGaAGTTTT	2	ATTTTGATATGCCAGCAGATACATG	CGCGACTACTGCTCCATTTG
CXCR4-Target4 OT44	GcCACCcAAAGGAGTTTT	2	CAGTCAACTTGTCCCATCAGC	CCTCCTTGCCCAAACACAATC
CXCR4-Target4 OT45	GTCACCaAAAGGAGTgTT	2	GCTTTCATTTGATTCAGCAGGTTG	TTCCCCATAGGCCTCAATGG
CXCR4-Target4 OT46	GTCAgCGAAAGGAGaTTT	2	ACGCAAGAATCACAACATGCC	TCATGCTTGTGTGAATCCAGG
CXCR4-Target4 OT47	GTCACaGAAAGGAGTTTg	2	GATGGACCAGCTGGAACTCC	GTTTGCTGCTGGAATCCTCC
CXCR4-Target4 OT48	GTCACCtAAAGGAGaTTT	2	CAGAGATCTGGGCCCCAATC	AGCTCAGAGGGCATGTGTTC
CXCR4-Target4 OT49	GTCcCCGAAAGGAGTgTT	2	TGGGGAGACAGTTCTGCTTTC	TCGAGGGAAAATGCTAGCCC
CXCR4-Target4 OT50	GTCACCtAAAGGAGTTcT	2	GGCATGTGAAATTCAGATTCTGC	CCCAGCAAACAGTAGGTAGTC
CXCR4-Target4 OT51	GTgACCGAAAGGAGTTTg	2	GTATCACTCGCAGTCGCCC	CTGCCGACGGTTATACCTCG
CXCR4-Target4 OT52	GTCACCGAAAGGAGcTaT	2	ATAGATGCCCTTTCGCAAGTC	TGCCAGAACAGTTGATTTCTATAGC
TTR-Target1 OT01	GTTCTAGATGCTGgCtGA	2	TTGAAGACAGTTCCCAGGGC	CAGGCACCTGTAACCTCCTC
TTR-Target1 OT02	GTTaTAGATGCTGTCCGt	2	CTGGTTGGTGCAGCTCTGTG	CCGGCTTTGAAATGAAGGGC
TTR-Target1 OT03	GTTCTAGATGCTGTatGA	2	TCATCATTCCAACCATAGGGCC	TGCAACTATCACCACAGCCC
TTR-Target1 OT04	GTTCTAGATGCTGTaCtA	2	CACACACACACACACACGAG	TCCCTCTGATGCATTGTGGC
TTR-Target1 OT05	GTTCTAGATGCTGagCGA	2	TGCATGCCTGTATTGAAACATCTC	TGGAAGTGTGAAGAGATACAAGTG
TTR-Target1 OT06	GTgaTAGATGCTGTCCGA	2	TTCTGTCTGCTGGCCTTCTC	TCCAGCATTGCCCGTTAGAG
TTR-Target1 OT07	cTTCTAGATGCTGTCCcA	2	TCGAGAGGAAATGTGAAGAGAGG	CAGCATCCCAGCAATTTTCCC
TTR-Target1 OT08	GTTCTAGATaCTGTCCaA	2	CCCTGACACAGTGATCTACAGG	AGTGTCACTTGATCTCTATGTGTC
TTR-Target1 OT09	GTaCTAGATGCTGTCCaA	2	ACATCTTACCCAGTCTCAAACAC	GCCCCATCCTTAGCAATTCC
TTR-Target1 OT10	GTgCTAGATGCTGTCCcA	2	TGTCCTTCTGCTACCTATCAAACC	TTTCCTCCTTGCATCTACCATAGAG
TTR-Target1 OT11	GTTCTAGATGtTGTCCtA	2	GGAGCAAATGATGGCAGCTG	TCCATGCAGTCTCCAATGCC

TTR-Target1 OT12	GTTtTtGATGCTGTCCGA	2	ACATAACCCCGCTTCTGTGG	TTCAGACCCCTACCTTACACC
TTR-Target1 OT13	GTTCTAGATtCTGTCCaA	2	CTACCCTGTACCTGGCACTG	GAGGGGCATTAACAGGAGGG
TTR-Target1 OT14	cTTCTAGATGCTGcCCGA	2	AGGGATTTTGCAGGTGTGATG	ACAGGGCTGTGTTCCTTCTG
TTR-Target1 OT15	GTTCTAGATGCTGTtCaA	2	TCAGCACTTAGTTGTGGGGC	AGCTGGGATTACAGGCACAC
TTR-Target1 OT16	GTTCTAGATGtTGTCCaA	2	TTTGGAGGCTGTGGAGTAGC	CTCCTTGCTCTCAGCTCCAG
TTR-Target1 OT17	tTTCTAGATGCTGTCCtA	2	TGCTGAAAGTAGGGCAGGTG	GTAATCTGCCTGCCTCAGCC
TTR-Target1 OT18	GTTtTAGATGCTaTCCGA	2	GTGGAAAGATGGGGAAGGGG	AACCCTGGAAAAGTAGGACTCAC
TTR-Target1 OT19	GTTCTAGAaGCTGTCCtA	2	ACCACTGGAGGAAATTGGGC	TCTTTTACCTCTTTTGCACCTCC
TTR-Target1 OT20	GTTCTAGATGCTaTCtGA	2	TTCAGCCTCCATGCCATCAG	TGTCTCTTCTCTGGATGCAGC
TTR-Target1 OT21	GTTCTAGATGCaGTCaGA	2	AGGCTATTATGCATTCAAACTGGC	AACCAGGGTGGAGAAGAAGC
TTR-Target1 OT22	cTTCTAGATGCTGTCCaA	2	TTCGTCCTGTGACTGCTTCC	GAGCTAGACACACTGCGAGG
TTR-Target1 OT23	GTTCTAGATGCTGTgCtA	2	ATCAGGCTAGGTCTGTGTCC	AGAGCCACCCACTTAGTGAG
TTR-Target1 OT24	GTaCTAGATGCTGTCCaA	2	GGACCATAGAAGACCCCAGG	TTGTCTGCATGACCCACTGG
TTR-Target1 OT25	tTTCTAGATGCTGTCCtA	2	AGGTGCTGGAATTACAGGCG	CTCATGGTCTTAGCCTGGGC
TTR-Target1 OT26	GTTCaAGATGCTGaCCGA	2	GGAGACACAAAAGGAATTGGGG	CCCACCAGTCCAGTTCCAAC
TTR-Target1 OT27	GTgCTAGATGCTGTCCtA	2	CCCCTCCCTCAGTCACTCTC	CCCCTAGCTGAGAATCACTGC
TTR-Target1 OT28	GTTCTAGATGCTtTCCtA	2	GGGGACAGGACATAAGTGGC	TCCAGATCCTTCCCTTCCCC
TTR-Target1 OT29	GTTCTAGcTGCTGTCtGA	2	GAAACAGGGGTGGGATGAGG	AGTAGGGGTACACCTTCAGC
TTR-Target1 OT30	tTTCTAGATGCTGTCtGA	2	CTATGCCCAAGCTCTCCGAC	AGCTTTCTTCCACCTAGGCC
TTR-Target1 OT31	GTTaTAGATGCTGTgCGA	2	GTGTGTGTGTGTGTGTGTGG	GAGCATGCAACACTCTGTGC
TTR-Target1 OT32	GgTCTAGATGCTGTCtGA	2	TCCCACTGCCACTTTCTTGC	TGATGGCTTTAAGAATGCGTTTG
TTR-Target1 OT33	tTTCTAGATGCTGTCCtA	2	TGCAATAGCTTTCCCAAAGGC	AGTGTGCTTCTCCAGACTGC
TTR-Target1 OT34	GTcCTAGATGCTGTCtGA	2	TAACCCCTGACCCATGTTGC	TGGCCTTTACTTCCTGGCAG
TTR-Target1 OT35	tTTCTAGATGCTGTCgGA	2	TACCTAAAGTGAGCCCAGCG	CGGGTGCTTTCTCTCCTCTC
TTR-Target1 OT36	GTTCTAGATGCTGgCCcA	2	AGTTCTCCTTCCTGAGCTGC	TTCTCTGTCCCTGGTCTCCC
TTR-Target1 OT37	GTTCTAGATaCTGTCaGA	2	GGGGATCTACACATTGCCCAATTC	TGACTGAAATGGTTTTCCTTTCCTG
TTR-Target1 OT38	GTTtTAGATGCTGTCCGc	2	TTTGCTGCTCTCTCCTTCCC	AAGGCCAAGTACACAGAGGC
TTR-Target1 OT39	GTTCTgGATGCTGTCaGA	2	TGCTTCCCAGACTGATGCTG	AGCAGCTGCCTGATTCTCTG
TTR-Target1 OT40	GTTCTAtATGCTGTCaGA	2	GAAAGCCCAAACACCATGGC	GGAGACTCCAGGCAGACTTC
TTR-Target1 OT41	GTTCTAGgTGCTGTCtGA	2	GCTCCATGTCTCTTGTTCTGC	AGTAATGCCGTGACTCACCAG
TTR-Target1 OT42	GTTCTAGAaGCTGTCaGA	2	CGTGTGAAAGGGAACAAGGC	TCTCCACTACCCCACAGGAG
TTR-Target1 OT43	GTTCTAcATGCTGTCtGA	2	ACTGTCTCATAAATAACTACCGCTG	CTCCCTGAAGGTCACAGCTG
TTR-Target1 OT44	cTTCTAGATGCTGTCCtA	2	AAACAGACACAGCCTCAGGG	ATTATTTTCCCCTCTGGCTGC
TTR-Target1 OT45	GTTCTAGAatCTGTCCGA	2	CAGTATGTGGGCAGCAGTTG	TCTCACTGCTGCTGCTACTAAC
TTR-Target1 OT46	GTTCTAGATGCaaTCCGA	2	AAGCAGGGAGGACTGAAAGC	GCCTCCTTTAATGGCCTCCC
TTR-Target1 OT47	GTaCTAGATGCTGTCCcA	2	CAAGTGTAAGGGTGCTGCTG	AGCCATGTGGAAGTTGGAGG
TTR-Target1 OT48	GTTCTAGATGtTGTaCGA	2	AGATTGGTGCTTGCCAGGG	TGTAGTGCCTAGAACATTGCC
TTR-Target4 OT01	GcACACATGCACGGgCAC	2	GTGTGCTTTTGTGTGTGTGC	TGACATGCAAAGTGCTGATGTG
TTR-Target4 OT02	GAACACATGCACGcaCAC	2	AGCCATAGCAACATCATGACAG	AGCTACAAGGGGAATAAGGCTG

TTR-Target4 OT03	GAAgACATGCAgGGCCAC	2	CTACATGAGGCCACACAGGG	TCACATCACCTTCCCATGGC
TTR-Target4 OT04	GAACACATGCACGcaCAC	2	ACTCTGCCACCTCAAGCTTC	CGAGATCATATGGGGCTTAGAAAAG
TTR-Target4 OT05	GAACACATGCAtGGCCAa	2	CACCTTCAGCCATTCTCACG	CAGAGTCTTGAGTAGGCACAATG
TTR-Target4 OT06	GcACACATGCACGGgCAC	2	AACTCCACCCTCATGTGTGC	CCAGTACGTCACAGTGGTGG
TTR-Target4 OT07	GAACACATGtAaGGCCAC	2	TCAGCCTCCCAAAGTGATAGT	AGTTCACAGGATATTCTGCAGGA
TTR-Target4 OT08	GtACACAcGCACGGCCAC	2	CATCACACACACACAGCCAC	ATGAAGCGCTCTCGTCTGAC
TTR-Target4 OT09	GAACACATGgACGGaCAC	2	ACAGGCCCCAGAGTGTAATG	GCAAAGACTTGGAACCAACCC
TTR-Target4 OT10	GgACACATGCACGGCCAg	2	GCCAGCTCTGTCTCCTGTAC	TGGCCACCTATAATCCAGGC
TTR-Target4 OT11	GcACACATGCACGGCCAC	1	ATCTGTCGAGTGGGTTGCAG	ACATGAGCCGTGTCTGAGTG
TTR-Target4 OT12	GAACACAgGCACaGCCAC	2	GAAAGGTCAAAACGGTCGGC	TGTGAGTGGGTGTGAGTGTG
TTR-Target4 OT13	GAAgACATtCACGGCCAC	2	TGGGTGTGAACGGGTGTTTC	CTCCAAGGGTCTGGTGTCTG
TTR-Target4 OT14	GAACACATGCACGcCCAC	1	CCCAACAGCTCAATTGCACC	TAAATGGGGTGGAGCACAGG
TTR-Target4 OT15	GAACACATGCACGGCCct	2	GGAAGGCCACTTGCATGAAC	GTGGGCAGCTCACAATTGTG
TTR-Target4 OT16	GcACACATaCACGGCCAC	2	AGCCAGGGACAACTTTCCAC	CATTCCACACACACAGCTGC
TTR-Target4 OT17	GAACACATcCAtGGCCAC	2	TGTCCTCACTACATGCACACTC	TGAACTCGTGGGCTCAAGTC
TTR-Target4 OT18	GAACACAgGCACGGCCAa	2	CTTACTGAGGGCGCTTCTCC	CCAACACGAGAGAGAGGCTG
TTR-Target4 OT19	GAACACATGCACGtaCAC	2	ACAGACACTACACGGGCATG	CTTCCACTCCTCACTGCTCC
TTR-Target4 OT20	GcACACATGCtCGGCCAC	2	TACTGTGCTGTGCTCTGGTG	CCCATCCTGAAGCTGACCTC
TTR-Target4 OT21	GAACACAcGCACGGCCAC	1	GGTCTCAAACTCCTGGGCTC	CTGTCCCTTATGAGGCCGAC
TTR-Target4 OT22	GAACACATGaACGaCCAC	2	GGACCAGACTCCAGACTTCC	ATCCACTATGACAGCAGCCC
TTR-Target4 OT23	GAACACATGtACGGCCAC	1	GATCACTTGAGCCCAGGAGG	AGGGTAAGATGCCAGTAGTAGC
TTR-Target4 OT24	GAACACATaCACGGaCAC	2	GGCACAGCGAAGAAGAAACG	GACTCTGAGGCTACCTGTGC
TTR-Target4 OT25	GgcCACATGCACGGCCAC	2	CCACCCTCACCAAGAGTCAC	CAACAATGACCTGTGGCTGC
TTR-Target4 OT26	GAACACATcCACGGtCAC	2	TGGTTCCCTCCTCTCACTCC	CCTAGGCTTGGTCCTGGTTC
TTR-Target4 OT27	GAACACATtCAaGGCCAC	2	CTTGCACATTGTGAGCCACC	GTTTCTGTGGGCCAGGAGTC
TTR-Target4 OT28	GAACACATGCcgGGCCAC	2	AGAACAGGGGATGGTGTTGG	GTGATCTACCCGCCTCAGC
TTR-Target4 OT29	GAACACAgGCACtGCCAC	2	CAGCACCTGGAGTTGAGAGG	CAGCAACCCCTTTGACAACG
TTR-Target4 OT30	GAACAggTGCACGGCCAC	2	AGAACATGGGTGAGTCCTGC	ATGCAGGTGCTGATGAGGAG
TTR-Target4 OT31	GAACACATGCAaGGCCAt	2	TCGACAGAACTACAGGGAGAAG	GGTTTGTTTGGTGCCTGTCC
TTR-Target4 OT32	GcACACATGCACGGCCAg	2	TCACAGACACAGCCATCTGG	CCACGCAAAATGAACCCCTC
TTR-Target4 OT33	GAACACAaGCACGGCaAC	2	AGCAGTCCCCGTTTATCCAC	ATCTTGGGCCATCTTGCTCC
TTR-Target4 OT34	GcACACATGCAgGGCCAC	2	CAGCTATTGCGTTGCAGTGG	TTTCCCTTCTGTCCCTGCTG
TTR-Target4 OT35	GAACACATGCACtGCaAC	2	GATGCGAAGGTCCTAGGGC	ACTTTCCATTTGAAGTCAGCAGC
TTR-Target4 OT36	GAACACATGCACaGtCAC	2	CTCCTACCATGCCAGTGCTG	CTGGGGTACTGGCCTTCATG
TTR-Target4 OT37	GAACACAgGCACtGCCAC	2	TGCAGGTGGGGATGATGAAC	CTCCTCGGGGAAAGGTGAAG
TTR-Target4 OT38	GAACACAgGCAgGGCCAC	2	TCTCTTCCCAAGAACCAGCG	TCAGCTCACGCACACCTTAG
TTR-Target4 OT39	GAACACATGCAtGcCCAC	2	AGGCTCCAGCTTACTCAAGG	TCCTGGAGGGCTTTTATACACAC
TTR-Target4 OT40	GcACACATGCACaGCCAC	2	ACAAGGTCACCTGACTGCTG	ATTGTCCTCGGTTCCAAGGC
TTR-Target4 OT41	GtACACATGCACGGaCAC	2	GCCAGCTTGTTTGTCATGGG	GTGATTCTCACCCTGGGAGC
TTR-Target4 OT42	GAACACATaCACaGCCAC	2	TCAGTCTTTCACACCCAGGC	TGGTTGAAATTCACTGAAATGG

				TG
TTR-Target4 OT43	GAACACtTGCAaGGCCAC	2	AGGGTGTGTCAGCATCCATG	GCTGATGGGGTGATTTCCAAC
TTR-Target4 OT44	GcACACATGCACGGaCAC	2	GGGCTTTCCTCCTTGCTTTC	CATCGTGTACAGTGCAGAGTG
TTR-Target4 OT45	GAACACAaGCACtGCCAC	2	TGTGATCTGAGCCAACCTGG	TGGAAGCCAAGGAAAGAGGG
TTR-Target4 OT46	cAACACATGCACaGCCAC	2	TGCCTACTCTTCCCTCCCAC	TAAGCCCAGCCTTTCTGTGG
TTR-Target4 OT47	GAACACATGCACtcCCAC	2	CTGGACAAAGAGCCCCTCTG	CTCCTGGCAGAATGAGGTGG
TTR-Target4 OT48	GAACACATGCAgGGCaAC	2	AAATGCATCGAGTGGCTTGC	ATTGGTCGGTAGTGTGGCTG
TTR-Target4 OT49	GAACACAgGCACtGCCAC	2	CCTCGGAGAAAGGTGAGAGG	TGCAGGTGGGGATGATGAAC
TTR-Target4 OT50	GAACACATaCACtGCCAC	2	TCGATTGGCCAAAGAACAGG	CTTTGGATTTCGTGAGGCGC
TTR-Target4 OT51	GAACACAgGCACtGCCAC	2	TCTTACCGCAGCACTTGGAG	GTTGTCACCTCTGAGCTGGG
TTR-Target4 OT52	GAACACATGCACGGagAC	2	AGCCAGTTTAGGTATGACTTTGG	ACCCTGTGGACTGTGAAAGC
TTR-Target4 OT53	GAACACATaCAaGGCCAC	2	CCCATGGCAGGCATTCAAAG	AGCAGATGTCAGCTCAGAGC
TTR-Target4 OT54	GAAgACATGCAaGGCCAC	2	CTCTGTGGGCTCTGGAGTTG	TGTGATGGAGTTGAAGTGGC
TTR-Target4 OT55	GgACACATGCACGGaCAC	2	GTAATCCGGGAGCACCACTC	TTGGATTCTCAGTGCGGAGG
TTR-Target4 OT56	GcACACATGCACaGCCAC	2	CGATGTGCCAATGTAGGTGC	TACAGGTGTGAGGCACTGTG
TTR-Target4 OT57	GAACACATGgAaGGCCAC	2	GAGCCCTGTCTCCTTCCTTG	TGCACGTGAATATTCATAGCAG C
TTR-Target4 OT58	GAACAgATGCAaGGCCAC	2	GAGGCCAGACCACAAGGATC	GTTTGCAGGAATGAGGCAGC
TTR-Target4 OT59	GAcCACATGCACaGCCAC	2	TCTGACCTGACTCCTTCCCC	TTCCGCTTGACTCTGTCTGG
TTR-Target4 OT60	GAACACATGCACtGCCAt	2	GCCCTAGAGCTGTCTCAGTTATC	TGTTTCGAGACTCCCAGTGG
TTR-Target4 OT61	GAACACAgGCACtGCCAC	2	AGGGGTTGAAAAGACAGGCC	ATGCTTTTGGCTGCAGTTGG
TTR-Target4 OT62	GAACACAaGCACtGCCAC	2	AGCTCTCTCTTTGCCTGCTG	AACTCTTGGGCTTTGGGGAC
TTR-Target4 OT63	GAACACtTGCcCGGCCAC	2	TGAGAGCAAACCAGATGCCC	GTCAGGGCTCAGGGTTTCTC
TTR-Target4 OT64	GAACACATGCctGGCCAC	2	GGGACTTGAGAACACCCCAC	TCACTGTGGTCTGAGAGTATGG
TTR-Target4 OT65	GAACAtAaGCACGGCCAC	2	TCTGATCCATTGCCTCCTGC	CTCAGCGACCTCAGCATTTG
TTR-Target4 OT66	GcACACATGCACGGCCAt	2	GCTATCTCTGTGGCCACCTC	GCCAGGCTGGTCTAGAACTC
TTR-Target4 OT67	GAACACATGgACGGaCAC	2	TAAGCCCCAAGTGCATTAGC	AGCTATCATTAATCAGAGTGGG TTG