

**Supplemental Table 1.**Sequences of the primers used for generation of  $\Delta$ H1/H6 virus

primer	Primer sequence
$\Delta$ miRNA-H1/6-kan-F	CGGAAAGCGGCGGGGTGTTGGGGGAGGCGAGGAACAACCGAGGGGAAGC TTCCTGATACCCATCCTACACAGGATGACGACGATAAGTA
$\Delta$ miRNA-H1/6-kan-R	GGGGCCGGAGGGTGGAAGGCAGGGGGTGTAGGATGGGTATCAGGAAAG CTCCCCTCGGTTGTTCCCTCGCAACCAATTAACCAATTCT
$\Delta$ miRNA-H1/6-zeo-F	CGGAAAGCGGCGGGGTGTTGGGGGAGGCGAGGAACAACCGAGGGGAATT CTGTTGACAATTAATCATCGGCAT
$\Delta$ miRNA-H1/6-zeo-R	GAGGGTGGAAGGCAGGGGGTGTAGGATGGGTATCAGGACTTCCACTTTC AGTCCTGCTCCTCGGCCA

**Supplemental Table 2.**

Sequences of the primers used to clone 3'UTR ATRX into pMIR-REPORT and to mutate the predicted target sites to generate pMIR-3'UTR ATRX-mut.

	primer	Primer sequence
PCR1	3'UTR-ATRX-1F	AAGAGCTCTGATTTTGCCTAAAAGCTTAATG
	3'UTR-ATRX-1R	TGGGAAAGTGGGGGAGAGGGGCGTGGATCCTT
PCR2	3'UTR-ATRX-2F	GAATTTGTGAGGTTTGGTGGATCCAA
	3'UTR-ATRX-2R	TTACGCGTCGGATTTAAACTTTATTACCCCA
	Mut_3'UTR-ATRX-Site1_F	GTAAACTAATACTCGAGATTGGCATTTAAG
	Mut_3'UTR-ATRX-Site1_R	AAATGCCAATCTCGAGTATTAGTTTTACTT
	Mut_3'UTR-ATRX-Site2_F	GTGGAGTTGTTACTATTGGTACCCGACTTGTTTTCACTGAA
	Mut_3'UTR-ATRX-Site2_R	TTCAGTGAAAACAAGTCGGGTACCAATAGTAACAACCTCCAC

**Supplemental Table 3.**

Sequences of oligonucleotide probes used for Northern blot analysis.

Target	Probe Sequences
miR-H1	ACTTCCACTTCCCGTCCT TCCATCCCCCGTTCCCC
miR-H3	TCCCAACCGCACAGTCCCAG
miR-H6	GGGGATGGAAGGACGGGAAGTGGA
<i>let-7a</i>	AACTATAACAACCTACTACCTCACCGGATCC
snRNA U6	AAAATATGGAACGCTTCACGA

**Supplemental Table 4.**

## Predicted human mRNA targets of HSV-1 miR-H1 and HSV-2 miR-H6

	Target GENE	Gene Name	Conserved sites			
			total	8mer	7mer-m8	7mer-1A
1	ATRX	alpha thalassemia/mental retardation syndrome X-linked (RAD54 homolog, <i>S. cerevisiae</i> )	2	2	0	0
2	BMPR2	bone morphogenetic protein receptor, type II (serine/threonine kinase)	2	2	0	0
3	TFRC	transferrin receptor (p90, CD71)	2	2	0	0
4	MOBK1A	MOB1, Mps One Binder kinase activator-like 1A (yeast)	2	1	1	0
5	PRKAA1	protein kinase, AMP-activated, alpha 1 catalytic subunit	2	1	1	0
6	TNRC6A	trinucleotide repeat containing 6A	2	1	1	0
7	C1orf21	chromosome 1 open reading frame 21	3	0	1	2
8	C18orf1	chromosome 18 open reading frame 1	2	0	2	0
9	KIF16B	kinesin family member 16B	2	0	2	0
10	LOC402665	hCG1651476	2	0	2	0
11	SPOPL	speckle-type POZ protein-like	2	0	2	0
12	ABHD2	abhydrolase domain containing 2	1	1	0	0
13	ADHFE1	alcohol dehydrogenase, iron containing, 1	1	1	0	0
14	ANKRD52	ankyrin repeat domain 52	1	1	0	0
15	ATG16L1	ATG16 autophagy related 16-like 1 ( <i>S. cerevisiae</i> )	1	1	0	0
16	ATXN1	ataxin 1	1	1	0	0
17	BAAT	bile acid Coenzyme A: amino acid N-acyltransferase (glycine N-choloyltransferase)	1	1	0	0
18	BRWD1	bromodomain and WD repeat domain containing 1	1	1	0	0
19	C5orf41	chromosome 5 open reading frame 41	1	1	0	0
20	CDK8	cyclin-dependent kinase 8	1	1	0	0
21	CNOT6	CCR4-NOT transcription complex, subunit 6	1	1	0	0
22	DKK3	dickkopf homolog 3 ( <i>Xenopus laevis</i> )	1	1	0	0
23	FAM136A	family with sequence similarity 136, member A	1	1	0	0
24	FAM150B	family with sequence similarity 150, member B	1	1	0	0
25	FBXW7	F-box and WD repeat domain containing 7	1	1	0	0
26	FGF11	fibroblast growth factor 11	1	1	0	0
27	GRIA2	glutamate receptor, ionotropic, AMPA 2	1	1	0	0
28	HDLBP	high density lipoprotein binding protein	1	1	0	0
29	ITGA9	integrin, alpha 9	1	1	0	0

30	KBTBD2	kelch repeat and BTB (POZ) domain containing 2	1	1	0	0
31	KDSR	3-ketodihydrosphingosine reductase	1	1	0	0
32	KLF12	Kruppel-like factor 12	1	1	0	0
33	KLF3	Kruppel-like factor 3 (basic)	1	1	0	0
34	KLF9	Kruppel-like factor 9	1	1	0	0
35	KLHL28	kelch-like 28 (Drosophila)	1	1	0	0
36	KPNA6	karyopherin alpha 6 (importin alpha 7)	1	1	0	0
37	LETM1	leucine zipper-EF-hand containing transmembrane protein 1	1	1	0	0
38	LIX1	Lix1 homolog (chicken)	1	1	0	0
39	LPHN2	latrophilin 2	1	1	0	0
40	MAPK1	mitogen-activated protein kinase 1	1	1	0	0
41	MRPS36	mitochondrial ribosomal protein S36	1	1	0	0
42	MYBPH	myosin binding protein H	1	1	0	0
43	NTRK2	neurotrophic tyrosine kinase, receptor, type 2	1	1	0	0
44	PAPPA	pregnancy-associated plasma protein A, pappalysin 1	1	1	0	0
45	PDE4D	phosphodiesterase 4D, cAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila)	1	1	0	0
46	PIM2	pim-2 oncogene	1	1	0	0
47	PTAR1	protein prenyltransferase alpha subunit repeat containing 1	1	1	0	0
48	PTP4A1	protein tyrosine phosphatase type IVA, member 1	1	1	0	0
49	PTPN20A	protein tyrosine phosphatase, non-receptor type 20A	1	1	0	0
50	PTPN20B	protein tyrosine phosphatase, non-receptor type 20B	1	1	0	0
51	RNF2	ring finger protein 2	1	1	0	0
52	SGK1	serum/glucocorticoid regulated kinase 1	1	1	0	0
53	SLC30A8	solute carrier family 30 (zinc transporter), member 8	1	1	0	0
54	SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4	1	1	0	0
55	SMG7	Smg-7 homolog, nonsense mediated mRNA decay factor (C. elegans)	1	1	0	0
56	SNX1	sorting nexin 1	1	1	0	0
57	SP3	Sp3 transcription factor	1	1	0	0
58	STK38L	serine/threonine kinase 38 like	1	1	0	0
59	USP46	ubiquitin specific peptidase 46	1	1	0	0
60	CAMKK2	calcium/calmodulin-dependent protein kinase kinase 2, beta	2	0	1	1
61	CBL	Cas-Br-M (murine) ecotropic retroviral transforming sequence	2	0	1	1
62	RTKN2	rhotekin 2	2	0	0	2
63	AAK1	AP2 associated kinase 1	1	0	1	0
64	ADO	2-aminoethanethiol (cysteamine) dioxygenase	1	0	1	0

65	AP3B1	adaptor-related protein complex 3, beta 1 subunit	1	0	1	0
66	ARHGAP21	Rho GTPase activating protein 21	1	0	1	0
67	ARHGAP5	Rho GTPase activating protein 5	1	0	1	0
68	ARID2	AT rich interactive domain 2 (ARID, RFX-like)	1	0	1	0
69	ATG4A	ATG4 autophagy related 4 homolog A ( <i>S. cerevisiae</i> )	1	0	1	0
70	ATP6V1A	ATPase, H <sup>+</sup> transporting, lysosomal 70kDa, V1 subunit A	1	0	1	0
71	ATXN7L3	ataxin 7-like 3	1	0	1	0
72	BASP1	brain abundant, membrane attached signal protein 1	1	0	1	0
73	BAZ2A	bromodomain adjacent to zinc finger domain, 2A	1	0	1	0
74	C16orf72	chromosome 16 open reading frame 72	1	0	1	0
75	C18orf25	chromosome 18 open reading frame 25	1	0	1	0
76	C21orf62	chromosome 21 open reading frame 62	1	0	1	0
77	CA7	carbonic anhydrase VII	1	0	1	0
78	CBX7	chromobox homolog 7	1	0	1	0
79	CD47	CD47 molecule	1	0	1	0
80	CNTN2	contactin 2 (axonal)	1	0	1	0
81	CORO1C	coronin, actin binding protein, 1C	1	0	1	0
82	CTNND1	catenin (cadherin-associated protein), delta 1	1	0	1	0
83	DDIT4	DNA-damage-inducible transcript 4	1	0	1	0
84	DGKI	diacylglycerol kinase, iota	1	0	1	0
85	DLG2	discs, large homolog 2, chapsyn-110 ( <i>Drosophila</i> )	1	0	1	0
86	DSTN	destrin (actin depolymerizing factor)	1	0	1	0
87	EGR3	early growth response 3	1	0	1	0
88	EPHA7	EPH receptor A7	1	0	1	0
89	FAM120A	family with sequence similarity 120A	1	0	1	0
90	FAS	Fas (TNF receptor superfamily, member 6)	1	0	1	0
91	FLJ13137	hypothetical gene supported by AK125122	1	0	1	0
92	FNDC4	fibronectin type III domain containing 4	1	0	1	0
93	FNDC5	fibronectin type III domain containing 5	1	0	1	0
94	FXR1	fragile X mental retardation, autosomal homolog 1	1	0	1	0
95	GATA6	GATA binding protein 6	1	0	1	0
96	GJC1	gap junction protein, gamma 1, 45kDa	1	0	1	0
97	GLI3	GLI-Kruppel family member GLI3 (Greig cephalopolysyndactyly syndrome)	1	0	1	0
98	GLUL	glutamate-ammonia ligase (glutamine synthetase)	1	0	1	0
99	GREB1	GREB1 protein	1	0	1	0

100	HIC1	hypermethylated in cancer 1	1	0	1	0
101	IRS1	insulin receptor substrate 1	1	0	1	0
102	ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)	1	0	1	0
103	JHDM1D	jumonji C domain containing histone demethylase 1 homolog D ( <i>S. cerevisiae</i> )	1	0	1	0
104	KCNMA1	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	1	0	1	0
105	KIAA0494	KIAA0494	1	0	1	0
106	KIAA1553	KIAA1553	1	0	1	0
107	KLF11	Kruppel-like factor 11	1	0	1	0
108	MAPKAP1	mitogen-activated protein kinase associated protein 1	1	0	1	0
109	MARK4	MAP/microtubule affinity-regulating kinase 4	1	0	1	0
110	MAST3	microtubule associated serine/threonine kinase 3	1	0	1	0
111	MBD2	methyl-CpG binding domain protein 2	1	0	1	0
112	MMP16	matrix metalloproteinase 16 (membrane-inserted)	1	0	1	0
113	MYLK4	myosin light chain kinase family, member 4	1	0	1	0
114	MYT1L	myelin transcription factor 1-like	1	0	1	0
115	NAV2	neuron navigator 2	1	0	1	0
116	NDST3	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 3	1	0	1	0
117	NFAT5	nuclear factor of activated T-cells 5, tonicity-responsive	1	0	1	0
118	NOVA1	neuro-oncological ventral antigen 1	1	0	1	0
119	NUMB	numb homolog ( <i>Drosophila</i> )	1	0	1	0
120	NXT2	nuclear transport factor 2-like export factor 2	1	0	1	0
121	OGT	O-linked N-acetylglucosamine (GlcNAc) transferase (UDP-N-acetylglucosamine: polypeptide-N-acetylglucosaminyl transferase)	1	0	1	0
122	PAN2	PAN2 polyA specific ribonuclease subunit homolog ( <i>S. cerevisiae</i> )	1	0	1	0
123	PARD6B	par-6 partitioning defective 6 homolog beta ( <i>C. elegans</i> )	1	0	1	0
124	PCGF5	polycomb group ring finger 5	1	0	1	0
125	PHC3	polyhomeotic homolog 3 ( <i>Drosophila</i> )	1	0	1	0
126	PIP4K2C	phosphatidylinositol-5-phosphate 4-kinase, type II, gamma	1	0	1	0
127	PLEKHA2	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 2	1	0	1	0
128	POLDIP2	polymerase (DNA-directed), delta interacting protein 2	1	0	1	0
129	PPP2R2A	protein phosphatase 2 (formerly 2A), regulatory subunit B, alpha isoform	1	0	1	0
130	PRKAB2	protein kinase, AMP-activated, beta 2 non-catalytic subunit	1	0	1	0
131	PTBP1	polypyrimidine tract binding protein 1	1	0	1	0
132	RAB11FIP4	RAB11 family interacting protein 4 (class II)	1	0	1	0
133	RAP2C	RAP2C, member of RAS oncogene family	1	0	1	0
134	RGS7BP	regulator of G-protein signaling 7 binding protein	1	0	1	0

135	RHEB	Ras homolog enriched in brain	1	0	1	0
136	RNF114	ring finger protein 114	1	0	1	0
137	RNF141	ring finger protein 141	1	0	1	0
138	RSRC2	arginine/serine-rich coiled-coil 2	1	0	1	0
139	SCMH1	sex comb on midleg homolog 1 (Drosophila)	1	0	1	0
140	7-Sep	septin 7	1	0	1	0
141	SFRS3	splicing factor, arginine/serine-rich 3	1	0	1	0
142	SH3GLB1	SH3-domain GRB2-like endophilin B1	1	0	1	0
143	SHANK2	SH3 and multiple ankyrin repeat domains 2	1	0	1	0
144	SHANK3	SH3 and multiple ankyrin repeat domains 3	1	0	1	0
145	SLC12A2	solute carrier family 12 (sodium/potassium/chloride transporters), member 2	1	0	1	0
146	SLC38A4	solute carrier family 38, member 4	1	0	1	0
147	SMURF1	SMAD specific E3 ubiquitin protein ligase 1	1	0	1	0
148	SNCA	synuclein, alpha (non A4 component of amyloid precursor)	1	0	1	0
149	SORT1	sortilin 1	1	0	1	0
150	SOX11	SRY (sex determining region Y)-box 11	1	0	1	0
151	SPATA2	spermatogenesis associated 2	1	0	1	0
152	TBC1D20	TBC1 domain family, member 20	1	0	1	0
153	TEAD1	TEA domain family member 1 (SV40 transcriptional enhancer factor)	1	0	1	0
154	TGOLN2	trans-golgi network protein 2	1	0	1	0
155	TMEM70	transmembrane protein 70	1	0	1	0
156	TNPO1	transportin 1	1	0	1	0
157	TNRC6B	trinucleotide repeat containing 6B	1	0	1	0
158	TRIM67	tripartite motif-containing 67	1	0	1	0
159	TTC7A	tetratricopeptide repeat domain 7A	1	0	1	0
160	TTL	tubulin tyrosine ligase	1	0	1	0
161	UBE2R2	ubiquitin-conjugating enzyme E2R 2	1	0	1	0
162	UHMK1	U2AF homology motif (UHM) kinase 1	1	0	1	0
163	UNK	unkempt homolog (Drosophila)	1	0	1	0
164	VDAC1	voltage-dependent anion channel 1	1	0	1	0
165	XPO1	exportin 1 (CRM1 homolog, yeast)	1	0	1	0
166	ZBTB39	zinc finger and BTB domain containing 39	1	0	1	0
167	ZFHX4	zinc finger homeobox 4	1	0	1	0
168	ZMIZ1	zinc finger, MIZ-type containing 1	1	0	1	0
169	ZNF294	zinc finger protein 294	1	0	1	0



170	ZNF828	zinc finger protein 828	1	0	1	0
171	ABCA1	ATP-binding cassette, sub-family A (ABC1), member 1	1	0	0	1
172	ABI3BP	ABI gene family, member 3 (NESH) binding protein	1	0	0	1
173	ADAMTS1	ADAM metalloproteinase with thrombospondin type 1 motif, 1	1	0	0	1
174	ADAMTS17	ADAM metalloproteinase with thrombospondin type 1 motif, 17	1	0	0	1
175	ADAT2	adenosine deaminase, tRNA-specific 2, TAD2 homolog ( <i>S. cerevisiae</i> )	1	0	0	1
176	AGMAT	agmatine ureohydrolase (agmatinase)	1	0	0	1
177	AOF1	amine oxidase (flavin containing) domain 1	1	0	0	1
178	ATP2B2	ATPase, Ca <sup>++</sup> transporting, plasma membrane 2	1	0	0	1
179	ATP2B4	ATPase, Ca <sup>++</sup> transporting, plasma membrane 4	1	0	0	1
180	C9orf40	chromosome 9 open reading frame 40	1	0	0	1
181	CAMK1	calcium/calmodulin-dependent protein kinase I	1	0	0	1
182	CAND1	cullin-associated and neddylation-dissociated 1	1	0	0	1
183	COL19A1	collagen, type XIX, alpha 1	1	0	0	1
184	CSNK2A2	casein kinase 2, alpha prime polypeptide	1	0	0	1
185	EPC2	enhancer of polycomb homolog 2 ( <i>Drosophila</i> )	1	0	0	1
186	EWSR1	Ewing sarcoma breakpoint region 1	1	0	0	1
187	FLRT1	fibronectin leucine rich transmembrane protein 1	1	0	0	1
188	FMR1	fragile X mental retardation 1	1	0	0	1
189	FOXF1	forkhead box F1	1	0	0	1
190	GLIS3	GLIS family zinc finger 3	1	0	0	1
191	GPATCH8	G patch domain containing 8	1	0	0	1
192	GRID1	glutamate receptor, ionotropic, delta 1	1	0	0	1
193	HNMT	histamine N-methyltransferase	1	0	0	1
194	HOOK3	hook homolog 3 ( <i>Drosophila</i> )	1	0	0	1
195	IGF1	insulin-like growth factor 1 (somatomedin C)	1	0	0	1
196	IKZF2	IKAROS family zinc finger 2 (Helios)	1	0	0	1
197	INPP5E	inositol polyphosphate-5-phosphatase, 72 kDa	1	0	0	1
198	KIAA0515	KIAA0515	1	0	0	1
199	KIAA2022	KIAA2022	1	0	0	1
200	KPNA1	karyopherin alpha 1 (importin alpha 5)	1	0	0	1
201	KPNA4	karyopherin alpha 4 (importin alpha 3)	1	0	0	1
202	LMOD1	leiomodulin 1 (smooth muscle)	1	0	0	1
203	LRRC2	leucine rich repeat containing 2	1	0	0	1
204	MAGI1	membrane associated guanylate kinase, WW and PDZ domain containing 1	1	0	0	1

205	MBNL1	muscleblind-like (Drosophila)	1	0	0	1
206	MEIS1	Meis homeobox 1	1	0	0	1
207	MKL2	MKL/myocardin-like 2	1	0	0	1
208	MON2	MON2 homolog (S. cerevisiae)	1	0	0	1
209	OAZ2	ornithine decarboxylase antizyme 2	1	0	0	1
210	PDIK1L	PDLIM1 interacting kinase 1 like	1	0	0	1
211	RNF165	ring finger protein 165	1	0	0	1
212	SAMD12	sterile alpha motif domain containing 12	1	0	0	1
213	SFRS12IP1	SFRS12-interacting protein 1	1	0	0	1
214	SFRS4	splicing factor, arginine/serine-rich 4	1	0	0	1
215	SLC23A2	solute carrier family 23 (nucleobase transporters), member 2	1	0	0	1
216	SLC38A1	solute carrier family 38, member 1	1	0	0	1
217	SMEK2	SMEK homolog 2, suppressor of mek1 (Dictyostelium)	1	0	0	1
218	SSBP3	single stranded DNA binding protein 3	1	0	0	1
219	SYT1	synaptotagmin I	1	0	0	1
220	TANC1	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 1	1	0	0	1
221	TNKS2	tankyrase, TRF1-interacting ankyrin-related ADP-ribose polymerase 2	1	0	0	1
222	VAV3	vav 3 guanine nucleotide exchange factor	1	0	0	1
223	XPO4	exportin 4	1	0	0	1
224	ZFYVE28	zinc finger, FYVE domain containing 28	1	0	0	1
225	ZFYVE9	zinc finger, FYVE domain containing 9	1	0	0	1
226	ZIC1	Zic family member 1 (odd-paired homolog, Drosophila)	1	0	0	1
227	ZNF664	zinc finger protein 664	1	0	0	1