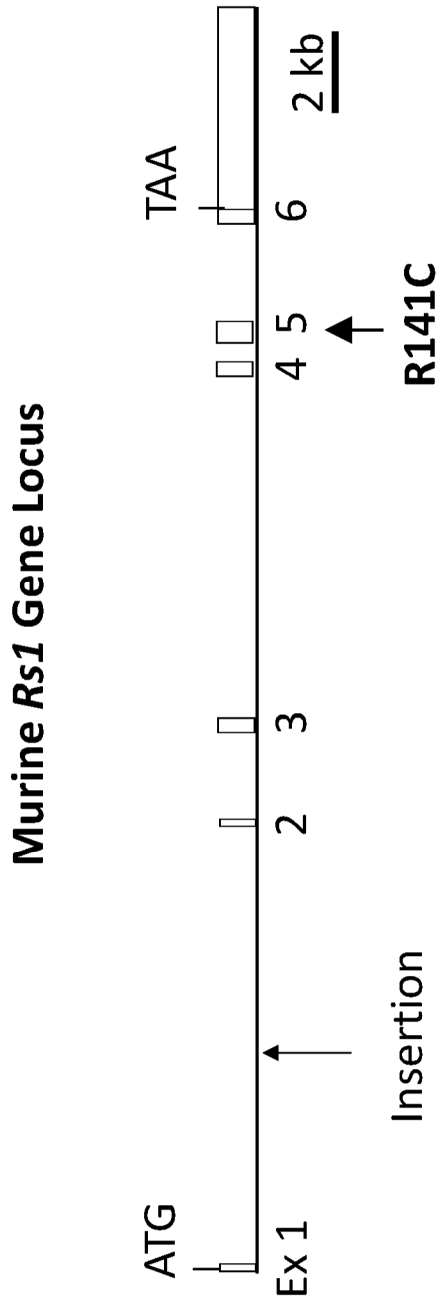


FIG. 1

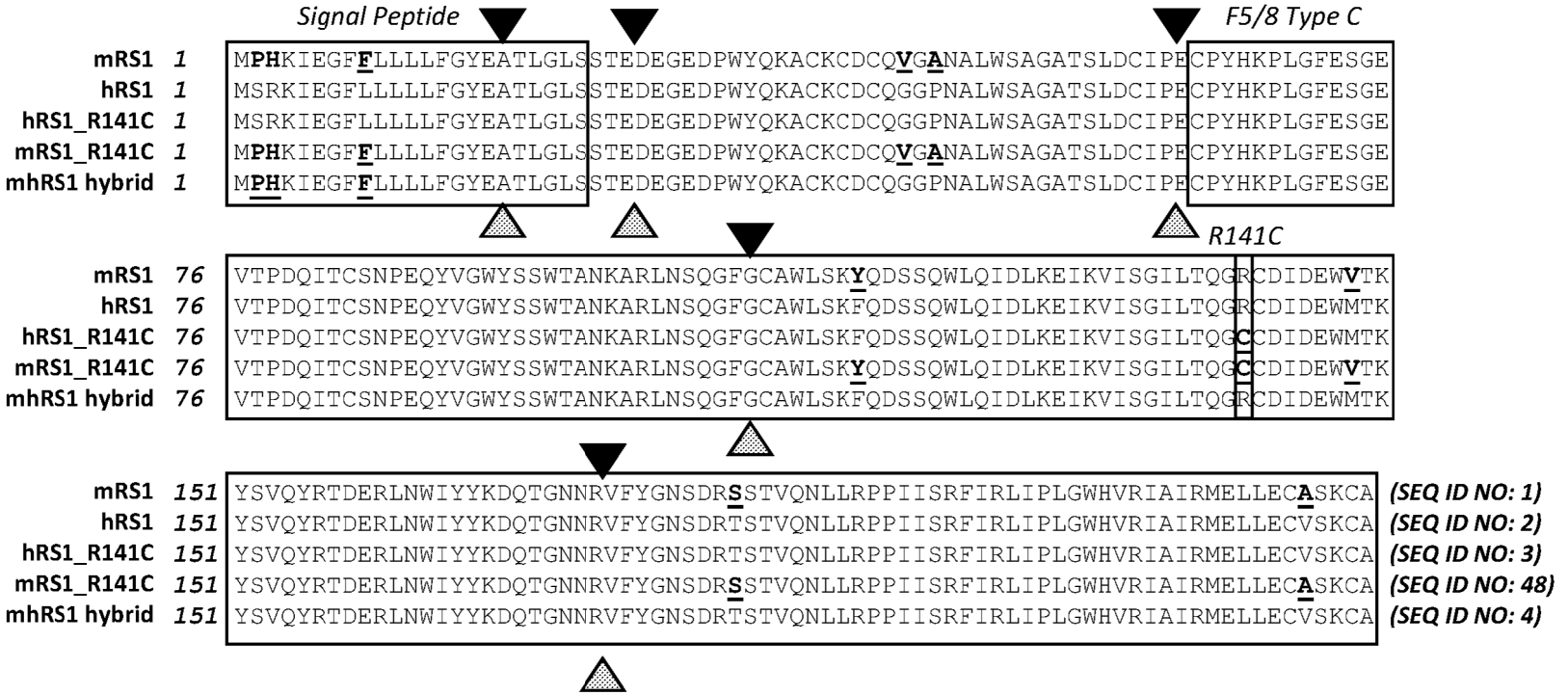

Signal Peptide
F5/8 Type C
R141C
mRS1 1 MPHKIEGFFLLLLFGYEATLGLSSTEDEGEDPWYQKACKCDCQVGANALWSAGATSLDCIPECPYHKPLGFESGE
hRS1 1 MSRKIEGFLLLLLFGYEATLGLSSTEDEGEDPWYQKACKCDCQGGPNALWSAGATSLDCIPECPYHKPLGFESGE
hRS1_R141C 1 MSRKIEGFLLLLLFGYEATLGLSSTEDEGEDPWYQKACKCDCQGGPNALWSAGATSLDCIPECPYHKPLGFESGE
mRS1_R141C 1 MPHKIEGFFLLLLFGYEATLGLSSTEDEGEDPWYQKACKCDCQVGANALWSAGATSLDCIPECPYHKPLGFESGE
mhRS1 hybrid 1 MPHKIEGFFLLLLFGYEATLGLSSTEDEGEDPWYQKACKCDCQGGPNALWSAGATSLDCIPECPYHKPLGFESGE
mRS1 76 VTPDQITCSNPEQYVGWYSSWTANKARLNSQGFGCAWLSKYQDSSQWLQIDLKEIKVISGILTQGRCDIDEWVTK
hRS1 76 VTPDQITCSNPEQYVGWYSSWTANKARLNSQGFGCAWLSKFQDSSQWLQIDLKEIKVISGILTQGRCDIDEWMTK
hRS1_R141C 76 VTPDQITCSNPEQYVGWYSSWTANKARLNSQGFGCAWLSKFQDSSQWLQIDLKEIKVISGILTQGCCDIDEWMTK
mRS1_R141C 76 VTPDQITCSNPEQYVGWYSSWTANKARLNSQGFGCAWLSKYQDSSQWLQIDLKEIKVISGILTQGCCDIDEWVTK
mhRS1 hybrid 76 VTPDQITCSNPEQYVGWYSSWTANKARLNSQGFGCAWLSKFQDSSQWLQIDLKEIKVISGILTQGRCDIDEWMTK
mRS1 151 YSVQYRTDERLNWIYYKDQTGNNRVFYGNSDRSSTVQNLLRPPIISRFIRLIPLGWHVRIAIRMELLECASKCA (SEQ ID NO: 1)
hRS1 151 YSVQYRTDERLNWIYYKDQTGNNRVFYGNSDRTSTVQNLLRPPIISRFIRLIPLGWHVRIAIRMELLECVSKCA (SEQ ID NO: 2)
hRS1_R141C 151 YSVQYRTDERLNWIYYKDQTGNNRVFYGNSDRTSTVQNLLRPPIISRFIRLIPLGWHVRIAIRMELLECVSKCA (SEQ ID NO: 3)
mRS1_R141C 151 YSVQYRTDERLNWIYYKDQTGNNRVFYGNSDRSSTVQNLLRPPIISRFIRLIPLGWHVRIAIRMELLECASKCA (SEQ ID NO: 48)
mhRS1 hybrid 151 YSVQYRTDERLNWIYYKDQTGNNRVFYGNSDRTSTVQNLLRPPIISRFIRLIPLGWHVRIAIRMELLECVSKCA (SEQ ID NO: 4)

FIG. 2

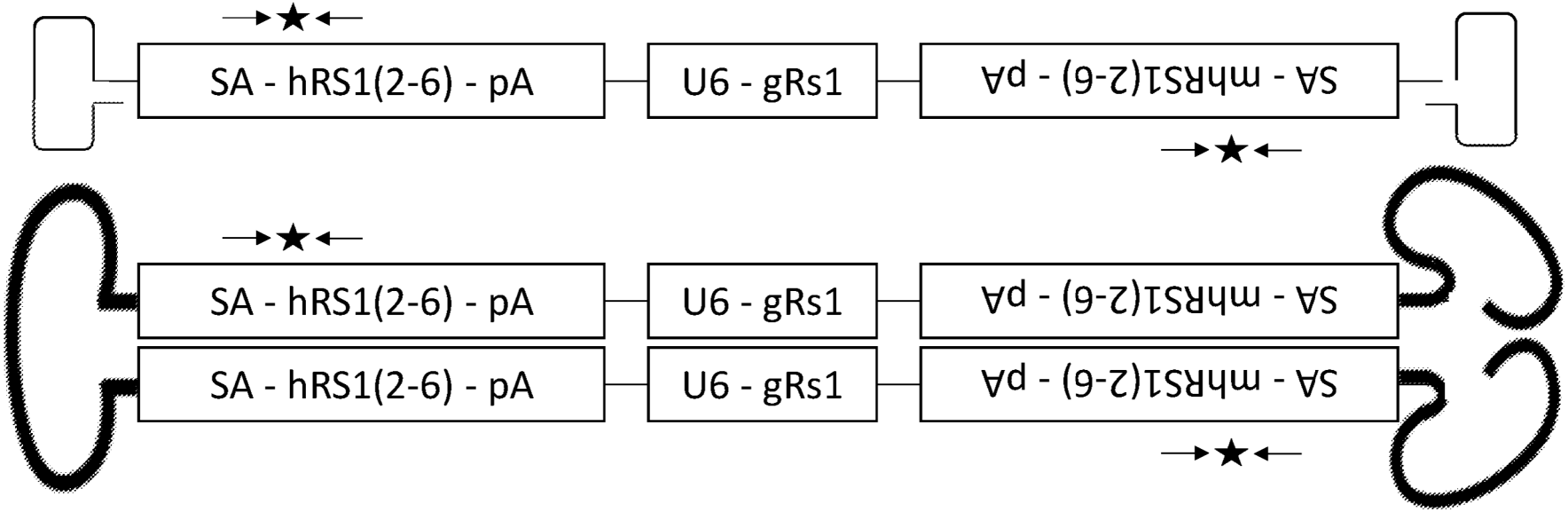

SA - hRS1(2-6) - pA
U6 - gRs1
SA - mhRS1(2-6) - pA
SA - hRS1(2-6) - pA
U6 - gRs1
SA - mhRS1(2-6) - pA
SA - hRS1(2-6) - pA
U6 - gRs1
SA - mhRS1(2-6) - pA

FIG. 3A

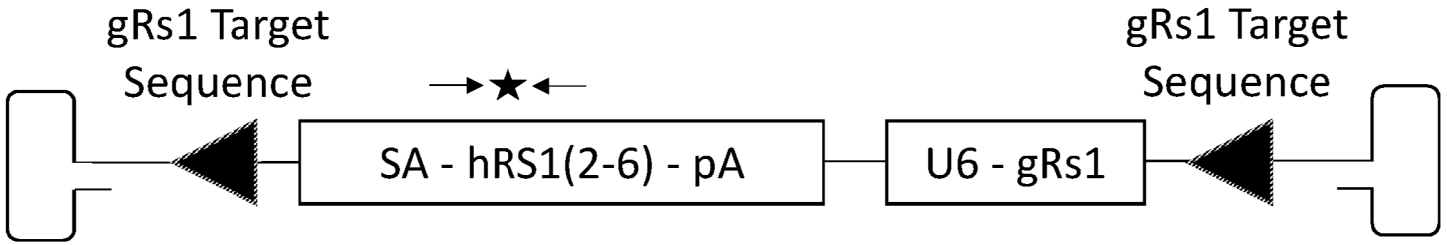
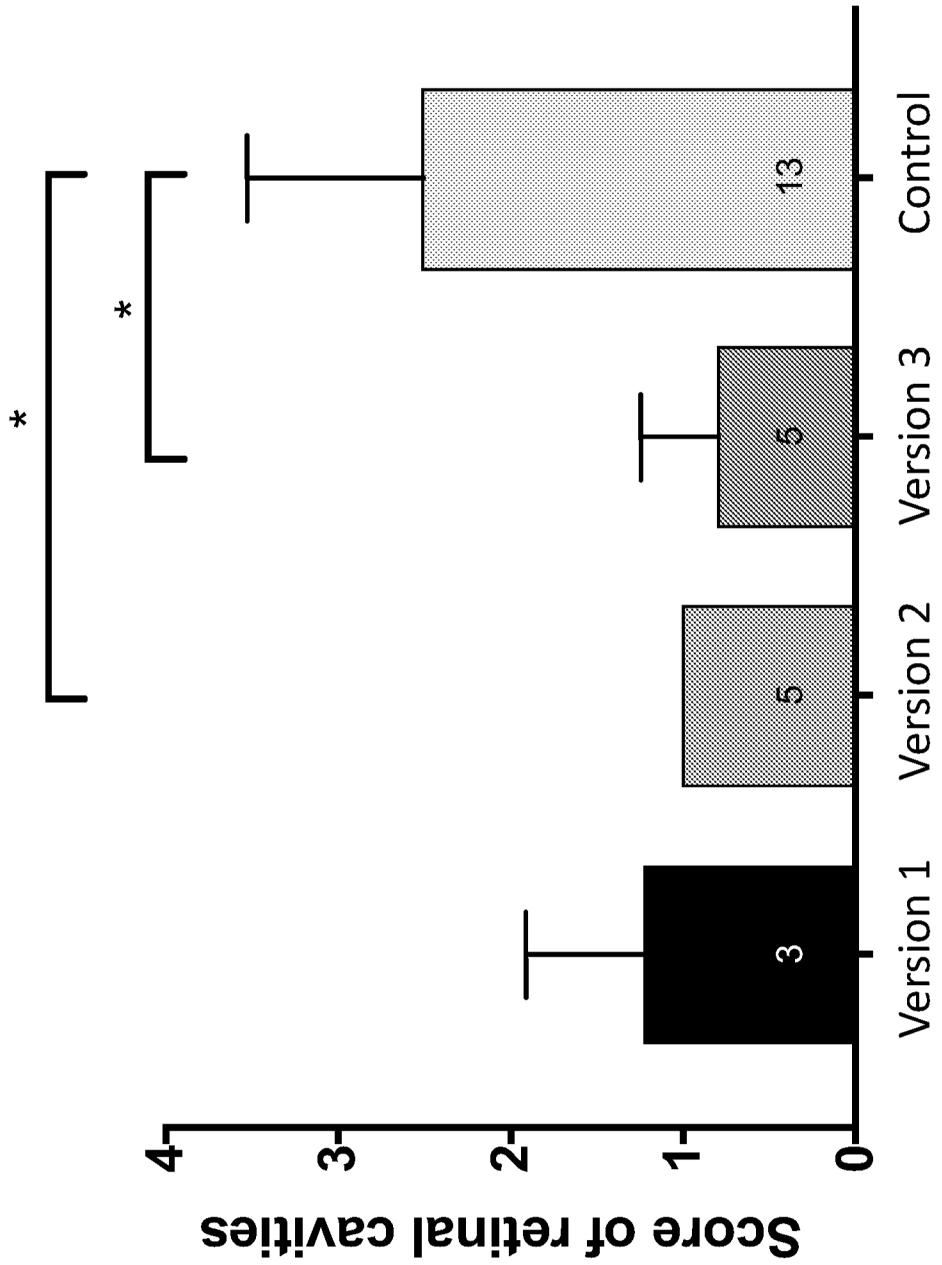

gRs1 Target Sequence
gRs1 Target Sequence
SA - hRS1(2-6) - pA
U6 - gRs1

FIG. 3B



Kruskal-Wallis test: p = 0.0023
Post hoc test: Dunn's multiple comparisons test

FIG. 4

AAV		Humanized Transcript 1		Humanized Transcript 2		Mutant Mouse		WT Mouse		Total Reads
		Read Count	Percent of Total Reads	Read Count	Percent of Total Reads	Read Count	Percent of Total Reads	Read Count	Percent of Total Reads	
pssAAV mhRS1-sgu	**6209**	4843	66%	1739	24%	793	11%			7375.00
	6210	925	68%	244	18%	201	15%			1370.00
	6211	1583	87%	0	0%	245	13%			1828.00
	6214	3037	41%	366	5%	547	7%	441	6%	7375.00
	6215	2946	40%	666	9%	713	10%	209	3%	7375.00
	6216	1561	21%	307	4%	202	3%	847	11%	7375.00
pscAAV rs1_tandem	**6228**	5460	80%	796	12%	541	8%			6797.00
	6229	3037	70%	860	20%	430	10%			4327.00
	6212	2085	83%	167	7%	267	11%			2519.00
	6230	2762	81%	266	8%	370	11%			3398.00
	6213	2295	64%	329	9%	947	27%			3571.00
	6225	1987	27%	0	0%	135	2%	349	5%	7375.00
	6266	1416	19%	125	2%	397	5%	337	5%	7375.00
	6267	1145	16%	64	1%	433	6%	1034	14%	7375.00
pssAAV hRs1_HITI	**6227**	3101	40%			4608	60%			7709.00
	6233	1599	47%			1770	53%			3369.00
	6231	3814	92%			324	8%			4138.00
	6226	425	12%			3081	88%			3506.00
	6232	4429	65%			2347	35%			6776.00
	6224	463	6%			3746	51%	356	5%	7375.00
	6222	1613	22%			2019	27%	1140	15%	7375.00
	6223	245	3%			211	3%	0	0%	7375.00

FIG. 5

Sample_ID	Gene	Mouse ID	Virus	Sex	Block	Well	Sample_ID	Gene	% INDEL	INDEL_READS	Total reads
S37	Rs1	4416227.00	7m8 hRS1_cDNA HITI	Male	Rs1_cDNA	B3	S339	Rs1	16.24	612.00	3768.00
S38	Rs1				Rs1_cDNA	B4	S340	Rs1	0.04	4.00	11396.00
S39	Rs1	4416233.00	7m8 hRS1_cDNA HITI	Male	Rs1_cDNA	B5	S341	Rs1	13.15	1575.00	11973.00
S40	Rs1				Rs1_cDNA	B6	S342	Rs1	0.25	21.00	8251.00
S41	Rs1	4416224.00	7m8 hRS1_cDNA HITI	Female	Rs1_cDNA	B7	S343	Rs1	10.68	2000.00	18721.00
S42	Rs1				Rs1_cDNA	B8	S344	Rs1	0.35	67.00	19102.00
S43	Rs1	4416231.00	7m8 hRS1_cDNA HITI	Male	Rs1_cDNA	F3	S371	Rs1	15.60	1143.00	7327.00
S44	Rs1				Rs1_cDNA	F4	S372	Rs1	0.03	3.00	10484.00
S45	Rs1	4416222.00	7m8 hRS1_cDNA HITI	Female	Rs1_cDNA	F5	S373	Rs1	2.28	750.00	32964.00
S46	Rs1				Rs1_cDNA	F6	S374	Rs1	0.06	12.00	21631.00
S47	Rs1	4416226.00	7m8 hRS1_cDNA HITI	Male	Rs1_cDNA	G1	S375	Rs1	44.36	4745.00	10697.00
S48	Rs1				Rs1_cDNA	G2	S376	Rs1	0.06	10.00	18139.00
S49	Rs1	4416232.00	7m8 hRS1_cDNA HITI	Male	Rs1_cDNA	G3	S377	Rs1	0.10	13.00	13314.00
S50	Rs1				Rs1_cDNA	G4	S378	Rs1	0.96	117.00	12153.00
S51	Rs1	4416223.00	7m8 hRS1_cDNA HITI	Female	Rs1_cDNA	G5	S379	Rs1	6.39	1218.00	19070.00
S52	Rs1				Rs1_cDNA	G6	S380	Rs1	0.06	10.00	17282.00
S61	Rs1	4416209.00	7m8 mhRS1-sgu	Male	Rs1_cDNA	B1	S337	Rs1	40.37	2558.00	6337.00
S62	Rs1				Rs1_cDNA	B2	S338	Rs1	0.06	4.00	7098.00
S63	Rs1	4416210.00	7m8 mhRS1-sgu	Male	Rs1_cDNA	C1	S345	Rs1	31.26	5276.00	16880.00
S64	Rs1				Rs1_cDNA	C2	S346	Rs1	0.20	19.00	9494.00
S65	Rs1	4416214.00	7m8 mhRS1-sgu	Female	Rs1_cDNA	C5	S349	Rs1	0.21	58.00	27275.00
S66	Rs1				Rs1_cDNA	C6	S350	Rs1	0.57	107.00	18717.00

FIG. 6A

S67	Rs1	4416211.00	7m8 mhRS1-sgu	Male	Rs1_cDNA	D1	S353	Rs1	0.16	18.00	11198.00
S68	Rs1				Rs1_cDNA	D2	S354	Rs1	2.95	241.00	8171.00
S69	Rs1	4416215.00	7m8 mhRS1-sgu	Female	Rs1_cDNA	D5	S357	Rs1	1.67	344.00	20657.00
S70	Rs1				Rs1_cDNA	D6	S358	Rs1	0.71	131.00	18442.00
S71	Rs1	4416216.00	7m8 mhRS1-sgu	Female	Rs1_cDNA	E5	S365	Rs1	10.05	1648.00	16399.00
S72	Rs1				Rs1_cDNA	E6	S366	Rs1	0.27	52.00	19225.00
S73	Rs1	4416228.00	7m8 pscAAV_rs1_tandem	Male	Rs1_cDNA	C3	S347	Rs1	10.14	1049.00	10346.00
S74	Rs1				Rs1_cDNA	C4	S348	Rs1	0.11	15.00	14040.00
S75	Rs1	4416225.00	7m8 pscAAV_rs1_tandem	Female	Rs1_cDNA	C7	S351	Rs1	32.82	4701.00	14325.00
S76	Rs1				Rs1_cDNA	C8	S352	Rs1	0.05	8.00	15328.00
S77	Rs1	4416229.00	7m8 pscAAV_rs1_tandem	Male	Rs1_cDNA	D3	S355	Rs1	32.67	4416.00	13519.00
S78	Rs1				Rs1_cDNA	D4	S356	Rs1	0.09	15.00	16677.00
S79	Rs1	4416226.00	7m8 pscAAV_rs1_tandem	Female	Rs1_cDNA	D7	S359	Rs1	19.87	3759.00	18917.00
S80	Rs1				Rs1_cDNA	D8	S360	Rs1	0.13	25.00	19461.00
S81	Rs1	4416212.00	7m8 pscAAV_rs1_tandem	Male	Rs1_cDNA	E1	S361	Rs1	0.07	8.00	11742.00
S82	Rs1				Rs1_cDNA	E2	S362	Rs1	0.17	21.00	12432.00
S83	Rs1	4416230.00	7m8 pscAAV_rs1_tandem	Male	Rs1_cDNA	E3	S363	Rs1	7.06	986.00	13974.00
S84	Rs1				Rs1_cDNA	E4	S364	Rs1	1.32	142.00	10767.00
S53	Rs1	4416227.00	7m8 pscAAV_rs1_tandem	Female	Rs1_cDNA	E7	S367	Rs1	1.48	260.00	17523.00
S54	Rs1				Rs1_cDNA	E8	S368	Rs1	0.39	63.00	16357.00
S55	Rs1	4416213.00	7m8 pscAAV_rs1_tandem	Male	Rs1_cDNA	F1	S369	Rs1	19.75	1286.00	6512.00
S56	Rs1				Rs1_cDNA	F2	S370	Rs1	0.28	24.00	8481.00

FIG. 6B

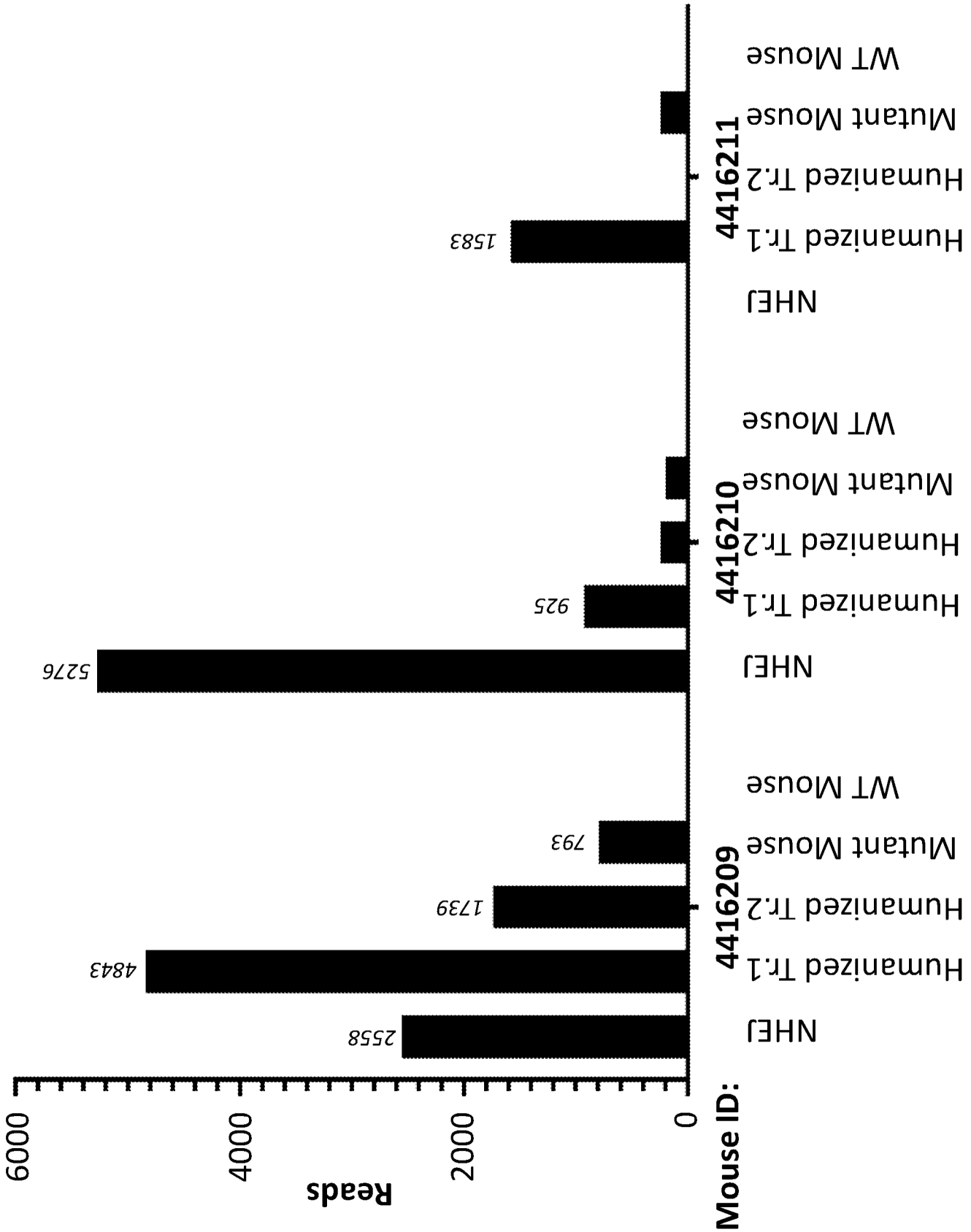

Reads
6000
4000
2000
0
Mouse ID:
NHEJ
Humanized Tr.1
Humanized Tr.2
Mutant Mouse
WT Mouse
4416209
2558
4843
1739
793
NHEJ
Humanized Tr.1
Humanized Tr.2
Mutant Mouse
WT Mouse
4416210
5276
925
NHEJ
Humanized Tr.1
Humanized Tr.2
Mutant Mouse
WT Mouse
4416211
1583

FIG. 7A

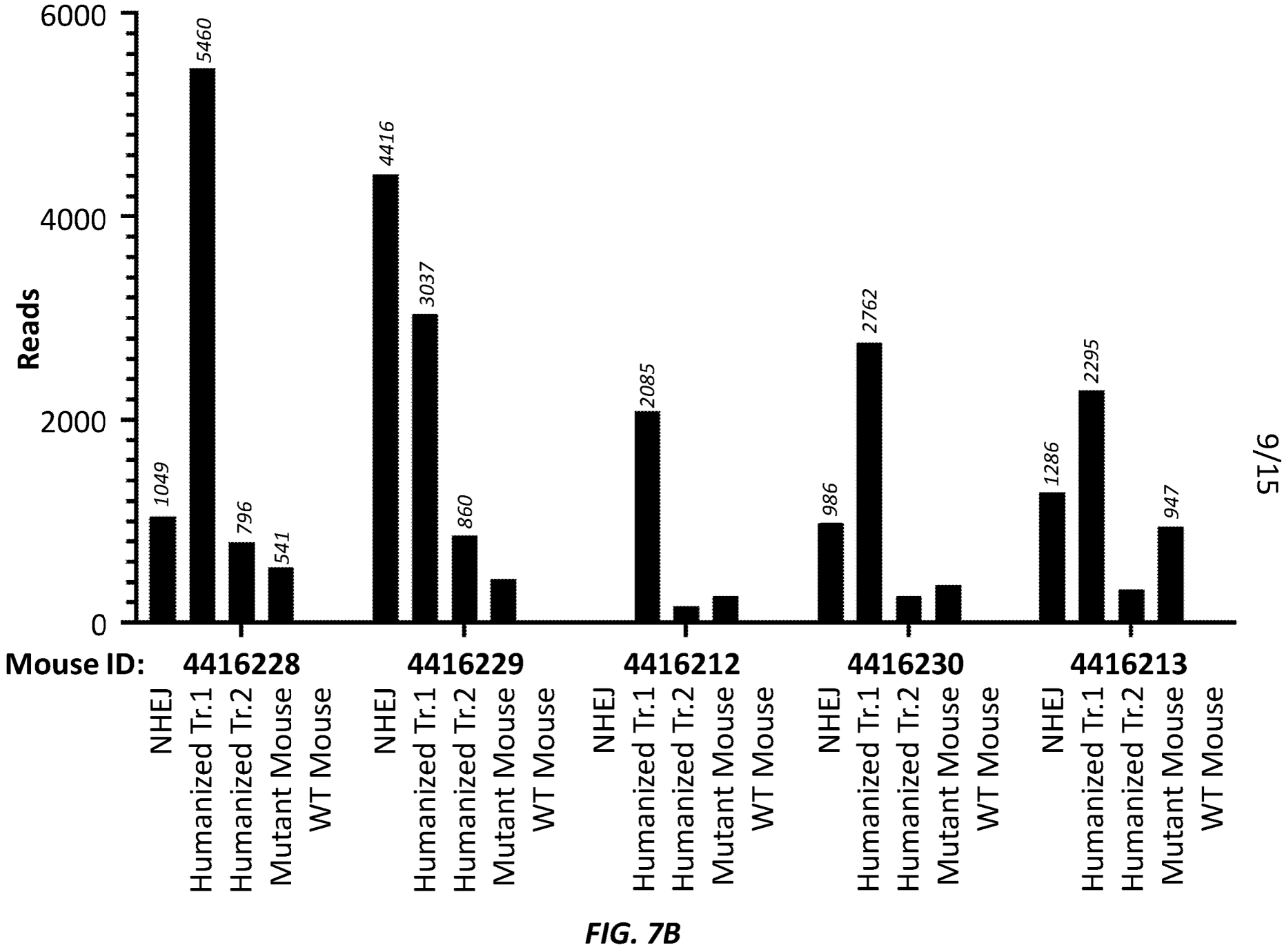

6000
4000
2000
0
Reads
1049
5460
796
541
4416
3037
860
2085
986
2762
1286
2295
947
Mouse ID:
4416228
4416229
4416212
4416230
4416213
NHEJ
Humanized Tr.1
Humanized Tr.2
Mutant Mouse
WT Mouse

FIG. 7B

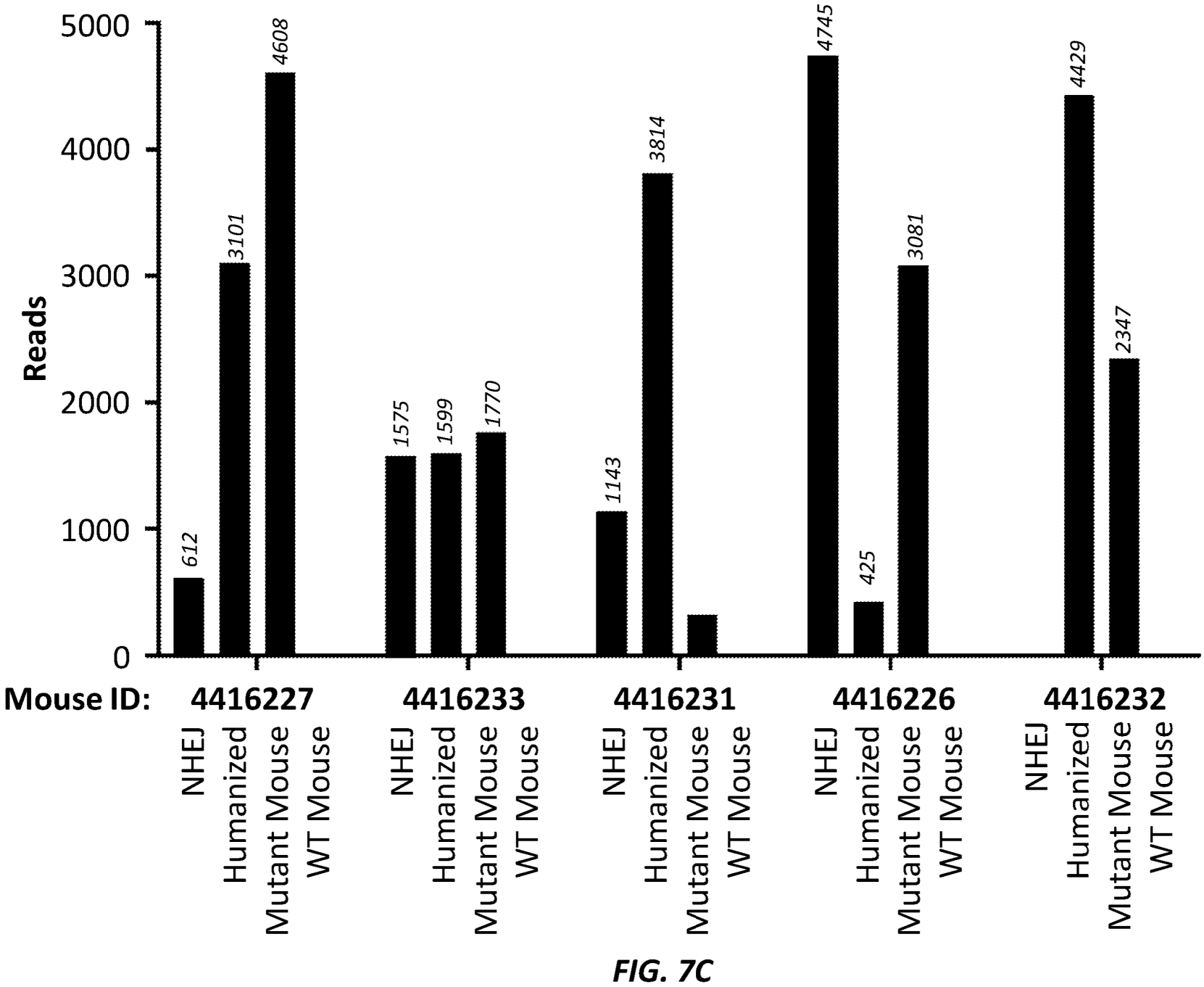

5000
4000
3000
2000
1000
0
Reads
612
3101
4608
1575
1599
1770
1143
3814
425
4745
3081
4429
2347
Mouse ID:
4416227
4416233
4416231
4416226
4416232
NHEJ
Humanized
Mutant Mouse
WT Mouse

FIG. 7C

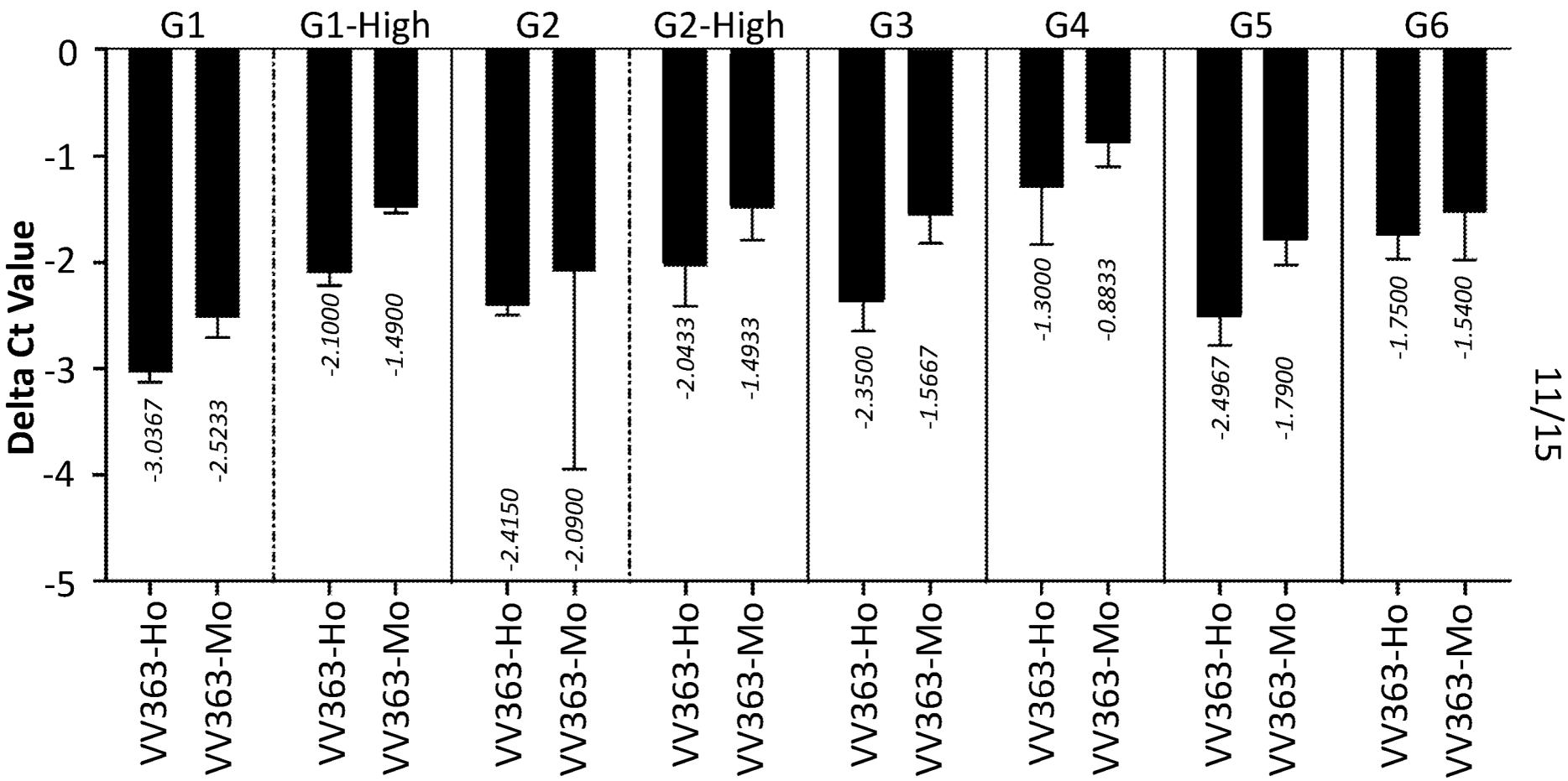

G1
G1-High
G2
G2-High
G3
G4
G5
G6
Delta Ct Value
0
-1
-2
-3
-4
-5
-3.0367
-2.5233
-2.1000
-1.4900
-2.4150
-2.0900
-2.0433
-1.4933
-2.3500
-1.5667
-1.3000
-0.8833
-2.4967
-1.7900
-1.7500
-1.5400
VV363-Ho
VV363-Mo
11/15

FIG. 8A

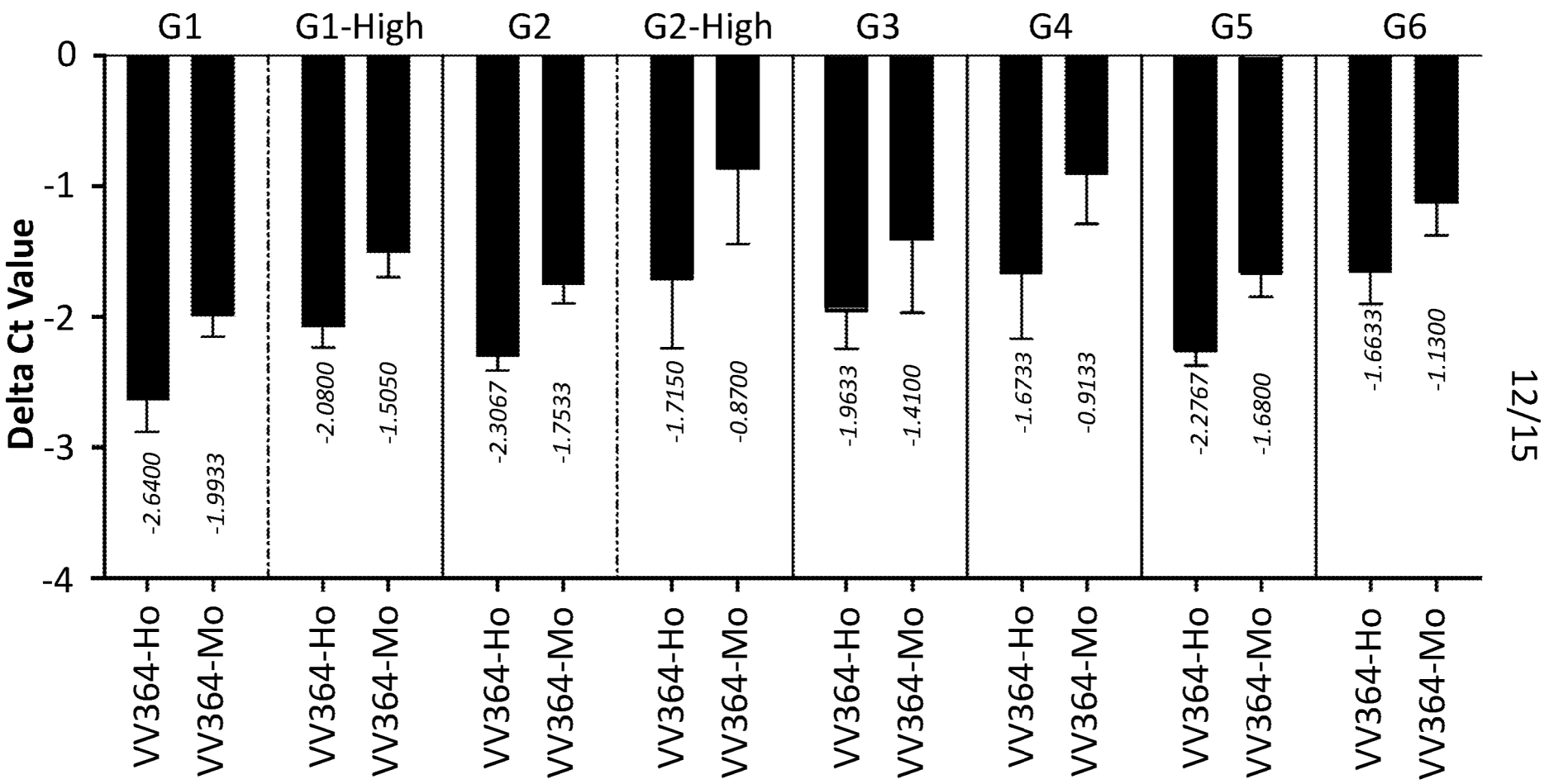

G1
G1-High
G2
G2-High
G3
G4
G5
G6
Delta Ct Value
0
-1
-2
-3
-4
-2.6400
-1.9933
-2.0800
-1.5050
-2.3067
-1.7533
-1.7150
-0.8700
-1.9633
-1.4100
-1.6733
-0.9133
-2.2767
-1.6800
-1.6633
-1.1300
VV364-Ho
VV364-Mo
12/15

FIG. 8B

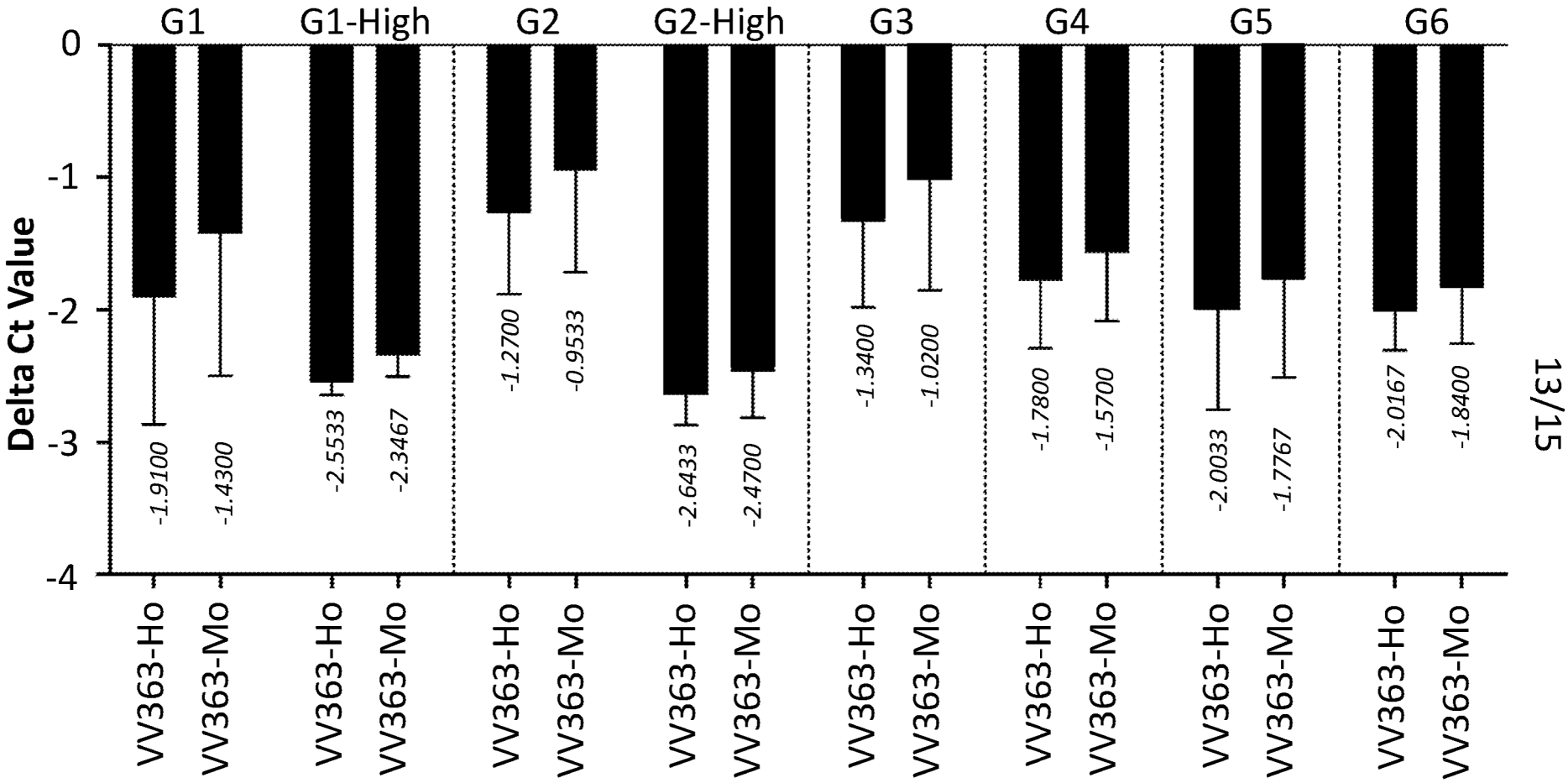

G1
G1-High
G2
G2-High
G3
G4
G5
G6
Delta Ct Value
0
-1
-2
-3
-4
-1.9100
-1.4300
-2.5533
-2.3467
-1.2700
-0.9533
-2.6433
-2.4700
-1.3400
-1.0200
-1.7800
-1.5700
-2.0033
-1.7767
-2.0167
-1.8400
VV363-Ho
VV363-Mo

FIG. 9A

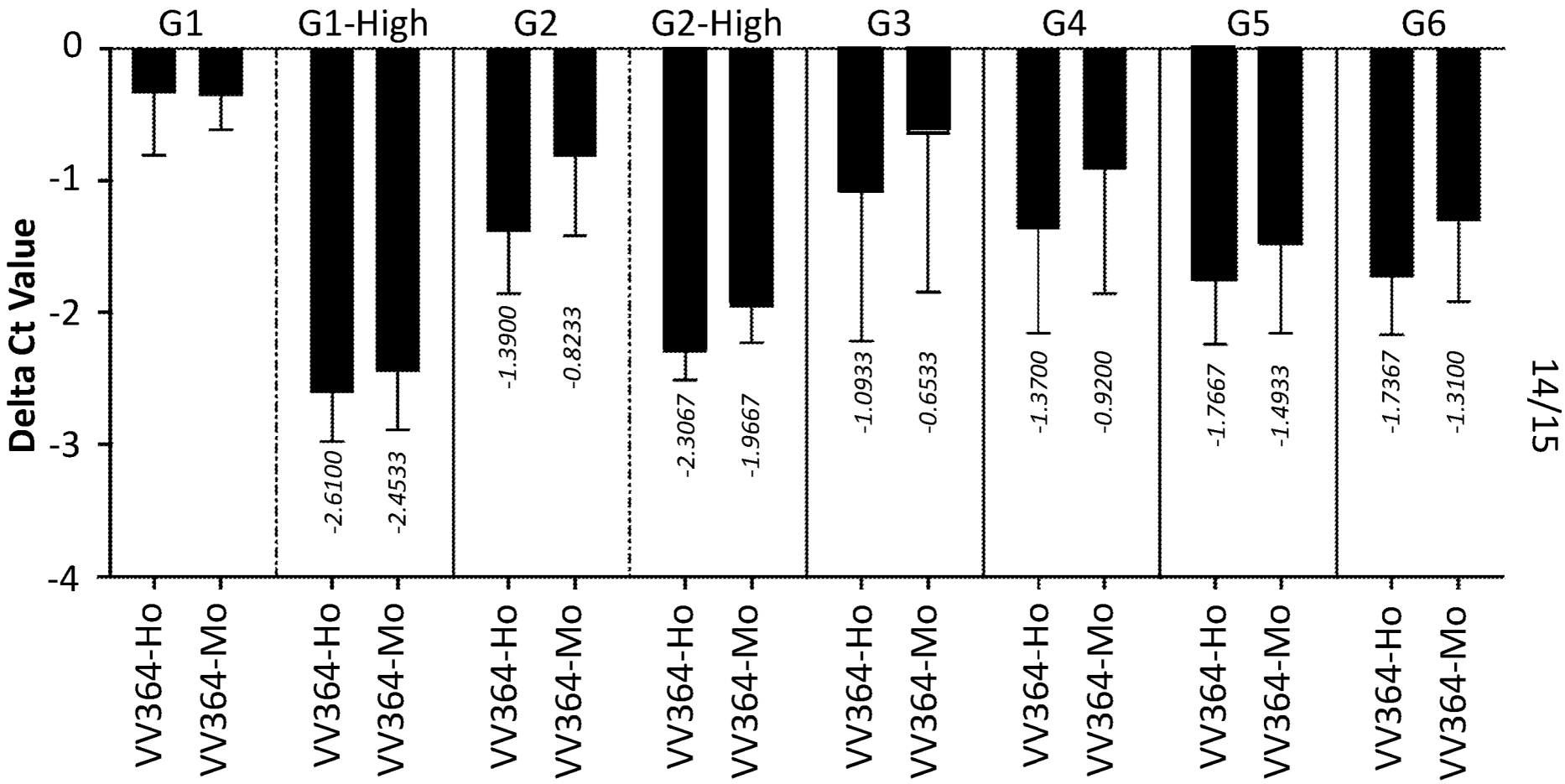

G1
G1-High
G2
G2-High
G3
G4
G5
G6
Delta Ct Value
0
-1
-2
-3
-4
-2.6100
-2.4533
-1.3900
-0.8233
-2.3067
-1.9667
-1.0933
-0.6533
-1.3700
-0.9200
-1.7667
-1.4933
-1.7367
-1.3100
VV364-Ho
VV364-Mo

FIG. 9B

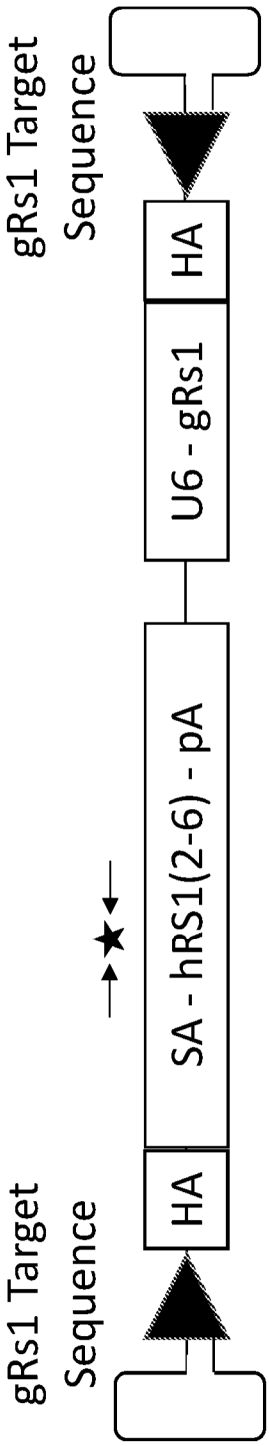

gRs1 Target Sequence
HA
SA - hRS1(2-6) - pA
U6 - gRs1
HA
gRs1 Target Sequence

FIG. 10