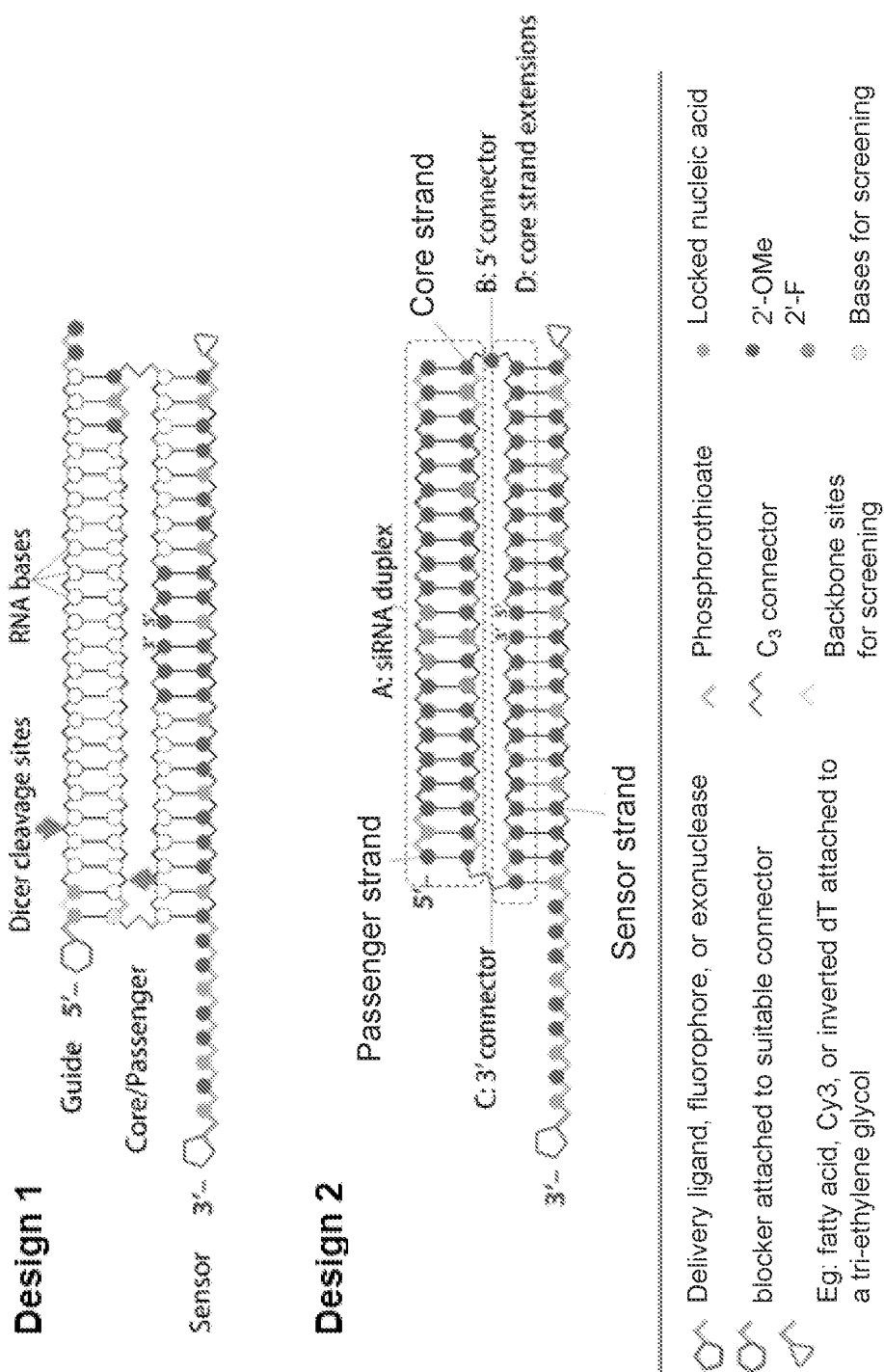




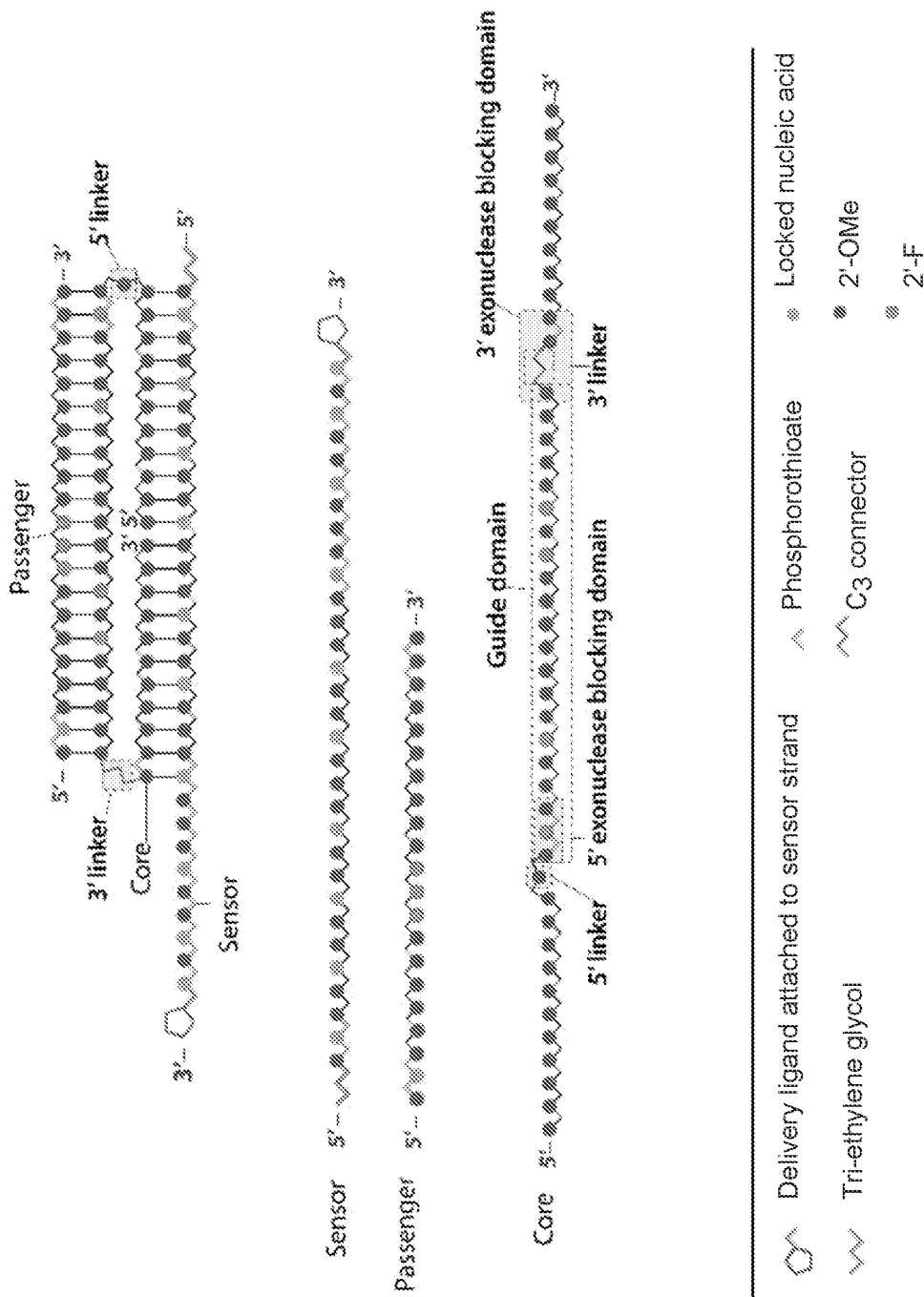
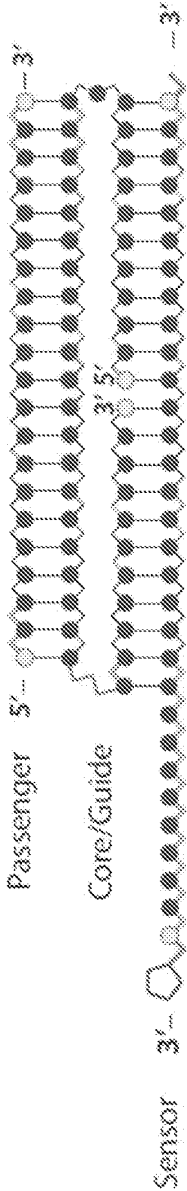


FIG. 2



	Delivery ligand, fluorophore, or exonuclease blocker attached to suitable connector Eg: fatty acid, Cy3, or inverted dT attached to a tri-ethylene glycol
	Phosphorothioate
	C ₃ connector
	Backbone sites for screening
	Locked nucleic acid
	2'-OMe
	2'-F
	Bases for screening

FIG. 3

Activation in targeted cells

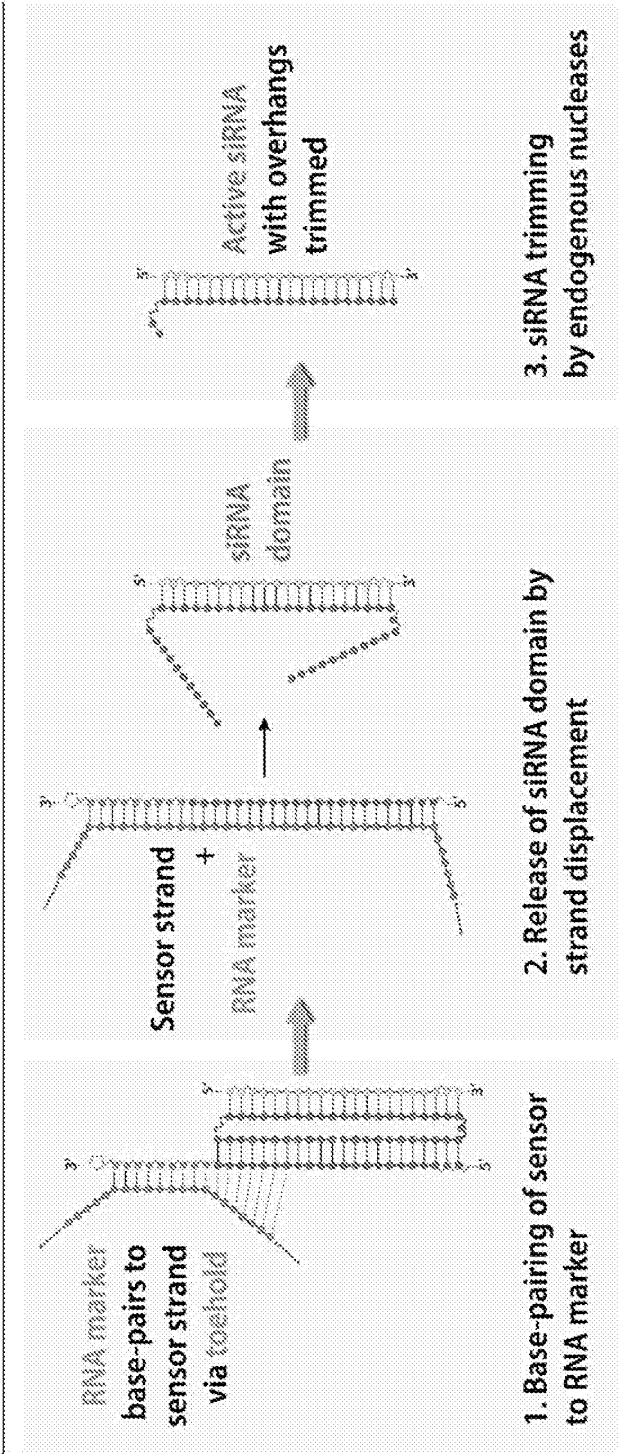


FIG. 4A

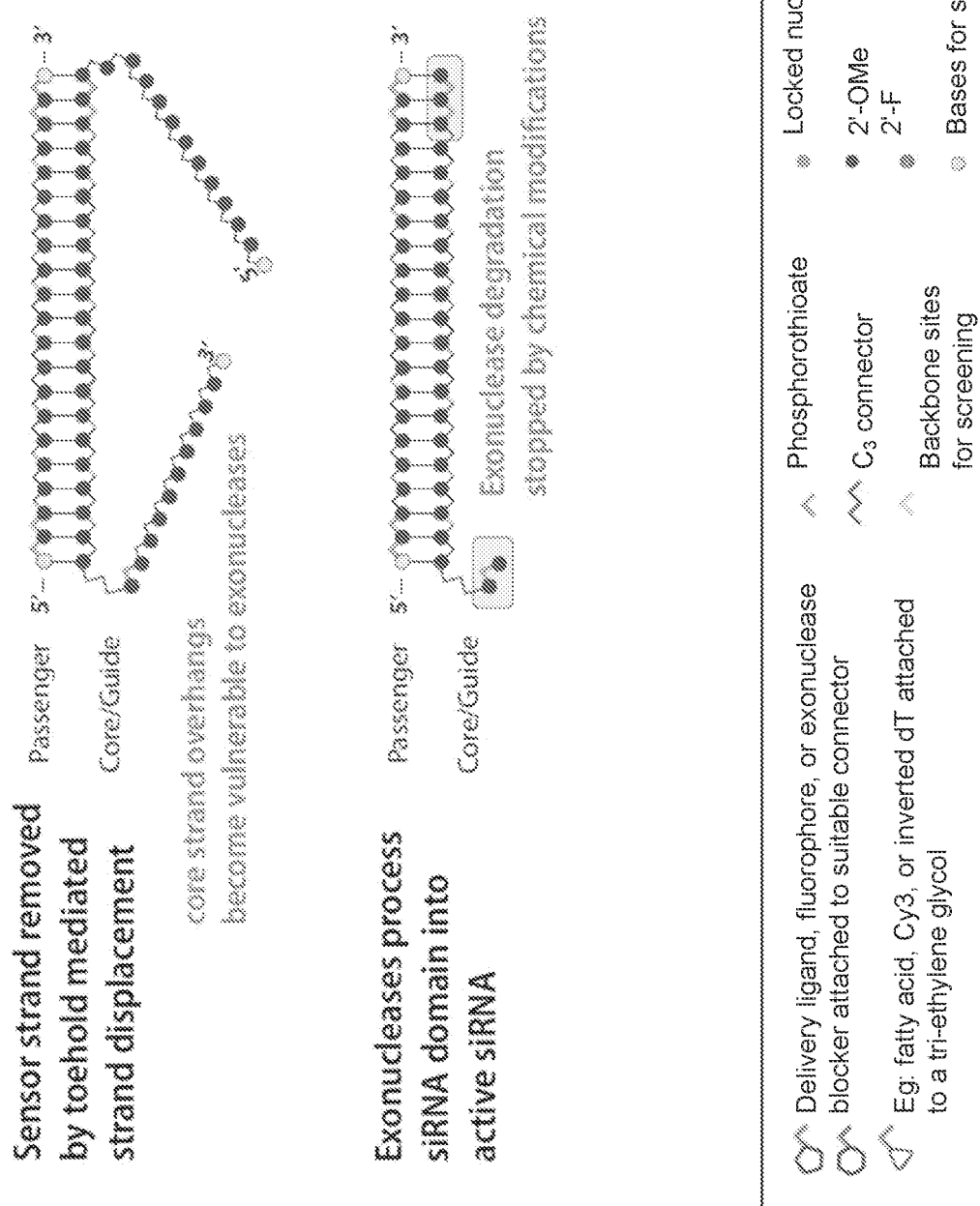


FIG. 4B

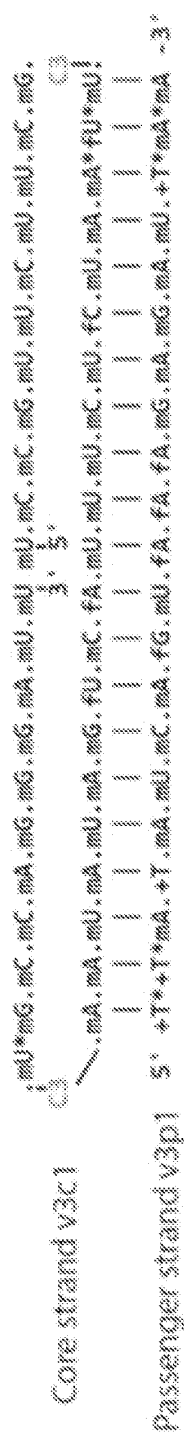


FIG. 5A

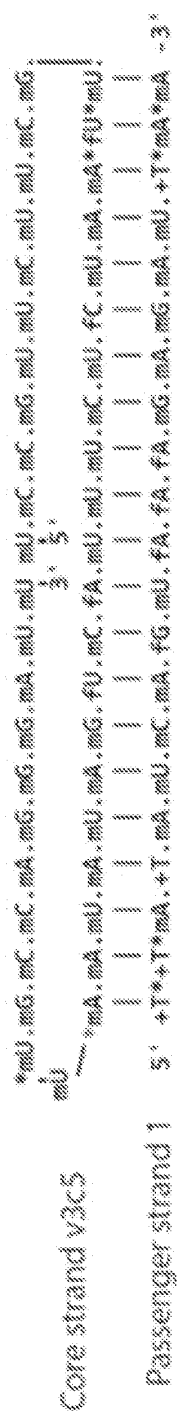


FIG. 5B

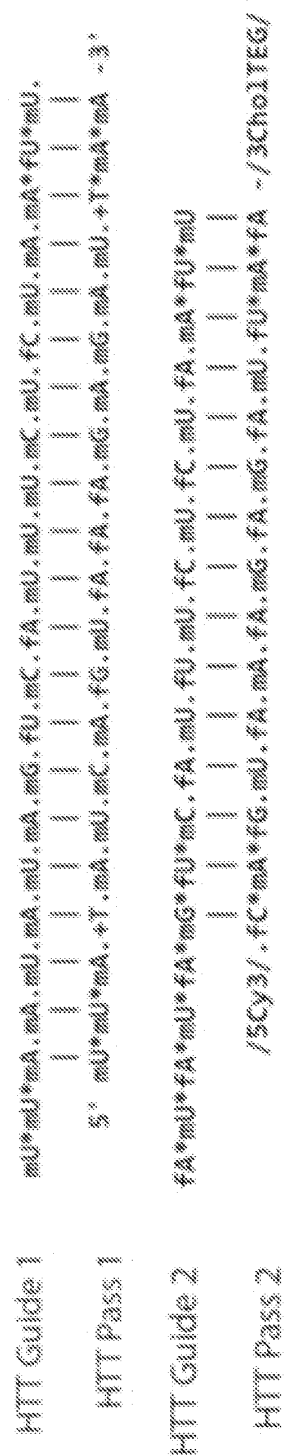


FIG. 6

Variant 3 strands		10 nM	1.0 nM	0.1 nM
siRNA 2	$fA^*mU^*fA^*mG^*fU^*mC.fA.mU.fU.mU.fC.mU.fC.mU.fA.mA^*fU^*mU$ $ $ $/5Cy3/.fC^*mA^*fG.mU.fA.mA.fA.mG.fA.mG.fA.mU.fU^*mA^*fA.-/3cho1fEG/$ (top: SEQ ID NO: 23; bottom: SEQ ID NO: 24)	0.48%	1.53%	31.87%
Passenger strand 1 siRNA 1	$mU^*mU^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 22)	1.03%	0.80%	3.50%
HIT V3P1	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 2)	32.47%	53.56%	86.64%
HIT V3P2	$/5Cy3/^*+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 25)	16.43%	27.19%	78.99%
HIT V3P3	$/5Sp9/^*+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 26)	33.13%	50.16%	84.28%
HIT V3P4	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA^*/3InvdI/$ (SEQ ID NO: 27)	25.36%	65.29%	95.21%
HIT V3P5	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA^*/3Cy3Sp/$ (SEQ ID NO: 28)	13.26%	40.09%	86.44%
HIT V3P6	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA^*/3Sp9/$ (SEQ ID NO: 29)	27.57%	56.74%	85.55%
HIT V3P7	$/5Cy3/^*+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA^*/3In$ $vdI/$ (SEQ ID NO: 30)	22.17%	52.90%	93.93%
HIT V3P8	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.mU.fA.fA.fA.+G.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 31)	92.19%	96.09%	99.78%
HIT V3P9	$+T^*+T^*mA.+T.mA.mU.mC.mA.fG.+T.fA.fA.fA.mG.mA.mG.mA.mU.+T^*mA^*mA$ (SEQ ID NO: 32)	22.01%	33.00%	70.07%

FIG. 7

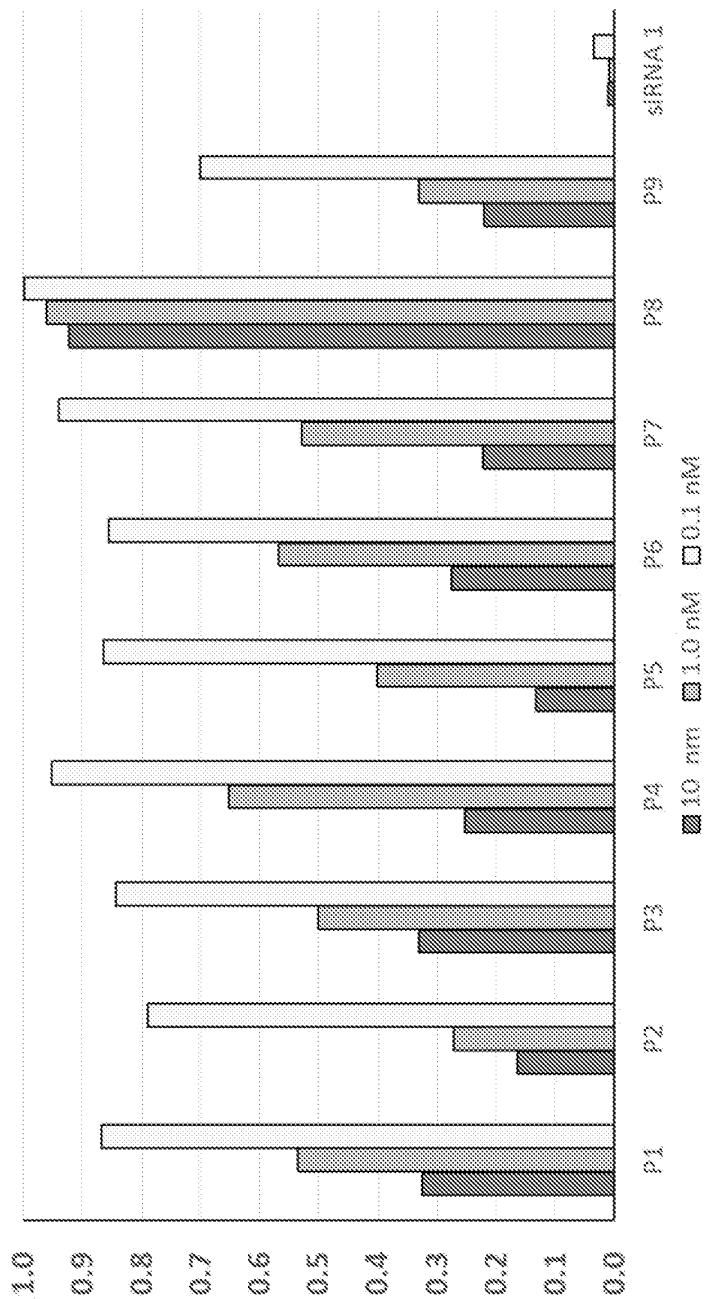


FIG. 8

Variant 3 strands		10 nM	1.0 nM	0.1 nM
siRNA 2	<i>fA</i>*mU*<i>fA</i>*mU*<i>fA</i>*mG*<i>fU</i>*mC, <i>fA</i>.mU. <i>fU</i>.mU. <i>fC</i>.mU. <i>fC</i>.mU. <i>fA</i>.mA*<i>fU</i>*mU /5<i>Cy3</i>/, <i>fC</i>*mA*<i>fG</i>.mU. <i>fA</i>.mA. <i>fA</i>.mG. <i>fA</i>.mG. <i>fA</i>.mU. <i>fU</i>*mA*<i>fA</i> ~ /3<i>Cho1</i>TEG/ (Top: SEQ ID NO: 23; Bottom: SEQ ID NO: 24)	0.48%	1.53%	31.87%
Passenger strand 1 siRNA 1	mU*mU*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 22)	1.03%	0.80%	3.50%
HTT V3P1	+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 2)	10.87%	1.10%	7.95%
HTT V3P2	/5<i>Cy3</i>/*+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 25)	3.04%	1.26%	8.51%
HTT V3P3	/5<i>Sp9</i>/*+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 26)	6.42%	0.96%	13.47%
HTT V3P4	+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA*/3<i>InvdT</i>/ (SEQ ID NO: 27)	3.26%	0.75%	7.85%
HTT V3P5	+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA*/3<i>Cy3</i>Sp/ (SEQ ID NO: 28)	4.38%	1.12%	7.92%
HTT V3P6	+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA*/3<i>Sp9</i>/ (SEQ ID NO: 29)	3.77%	0.83%	5.31%
HTT V3P7	/5<i>Cy3</i>/*+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA*/3<i>InvdT</i>/ (SEQ ID NO: 30)	2.85%	1.01%	11.53%
HTT V3P8	+T*+T*mA. +T mA.mU.mC.mA.fG.mU.fA.fA.fA. +G.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 31)	32.01%	3.21%	13.51%
HTT V3P9	+T*+T*mA. +T mA.mU.mC.mA.fG. +T.fA.fA.fA.mG.mA.mG.mA.mU. +T*mA*mA (SEQ ID NO: 32)	4.20%	0.97%	4.13%

Fig. 9

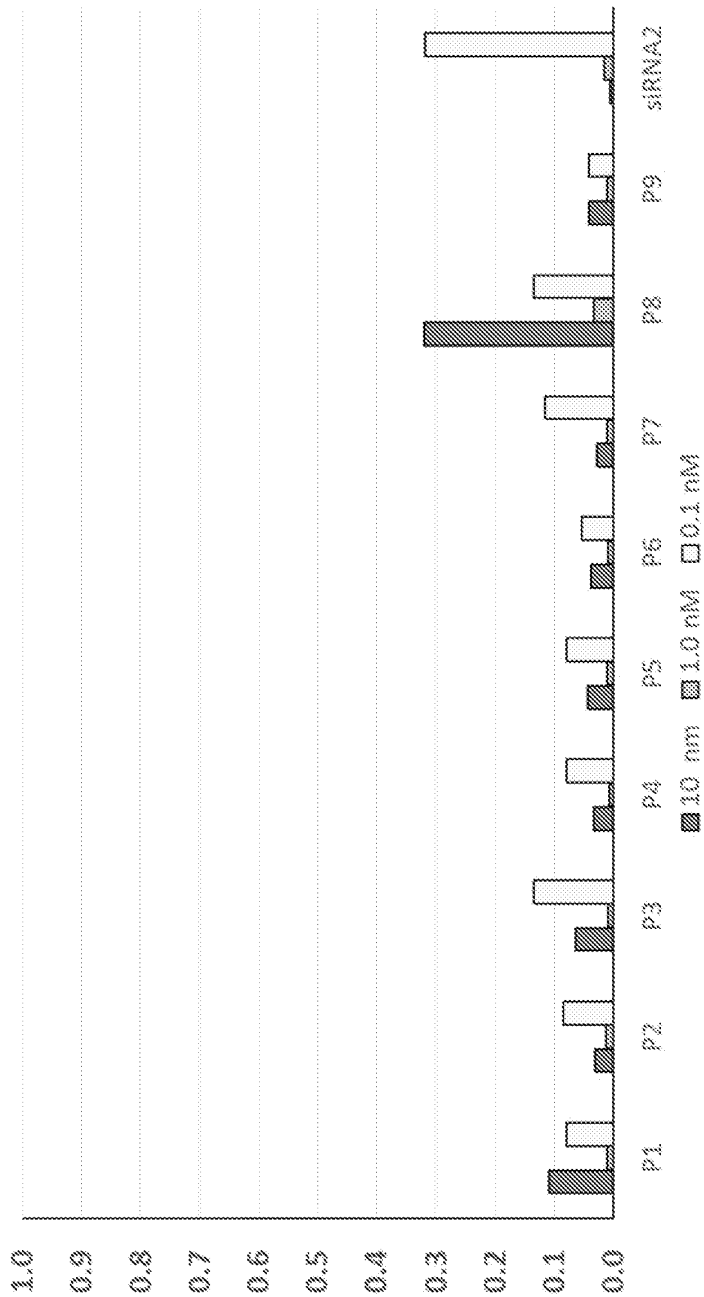


FIG. 10

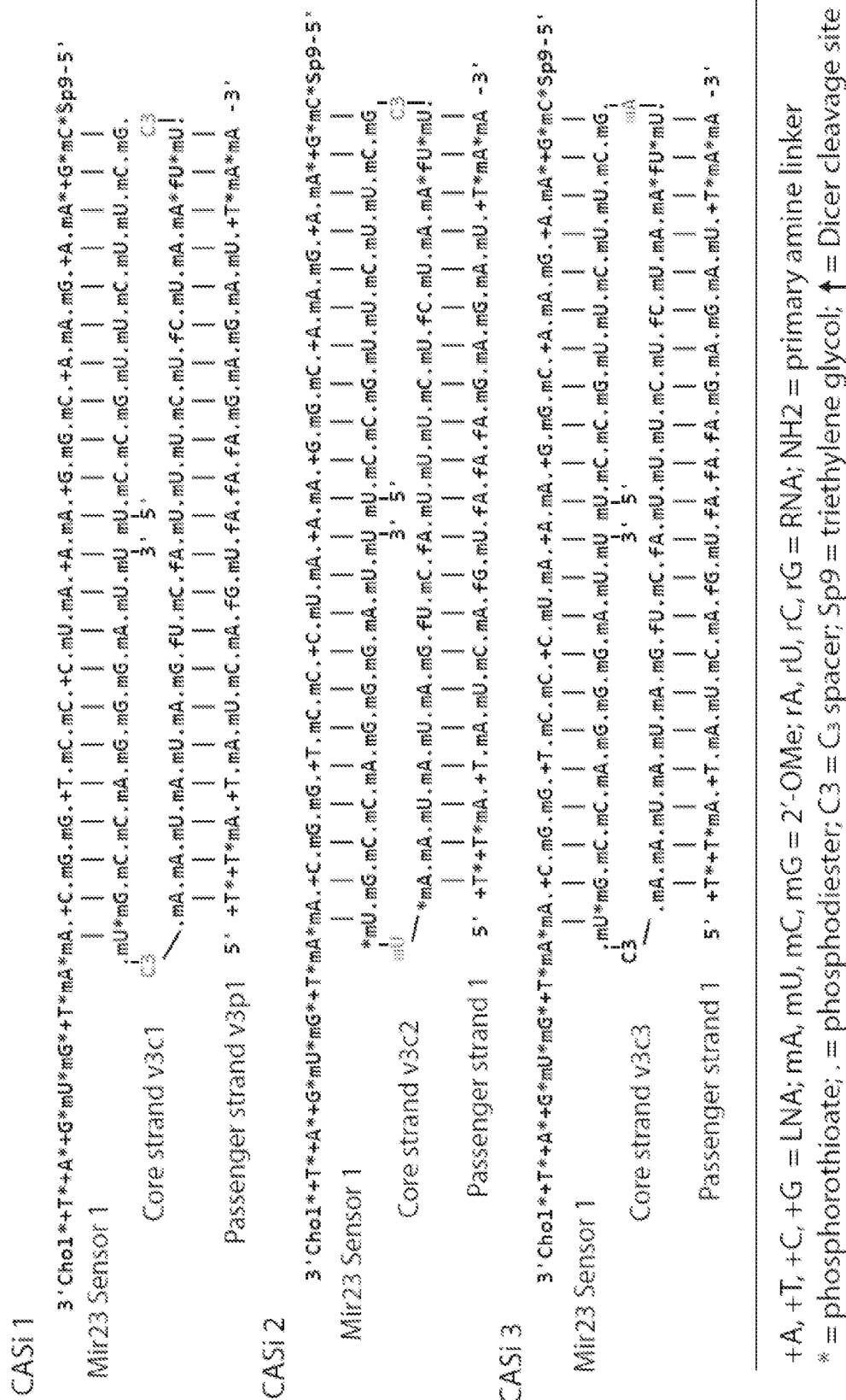


FIG. 11A

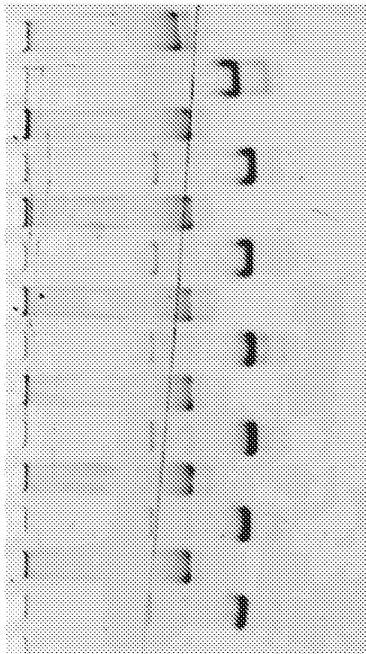


FIG. 12

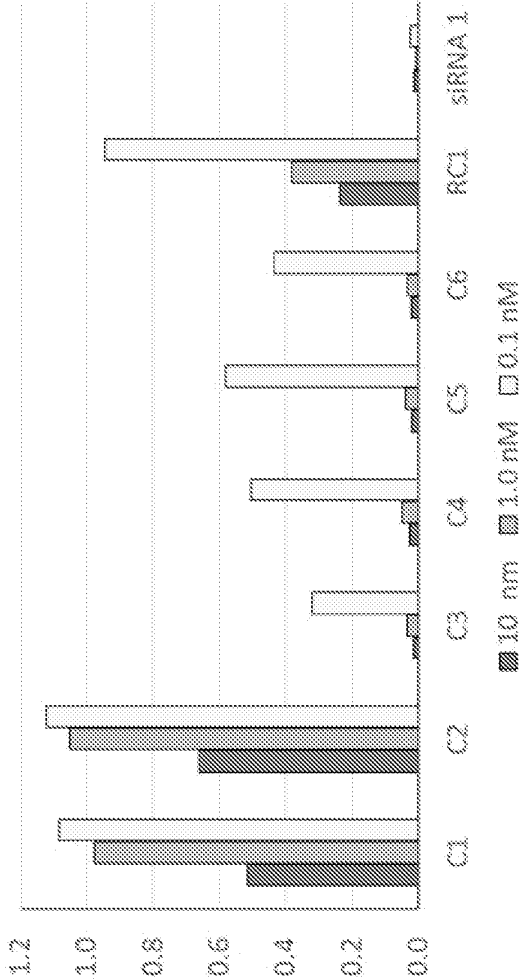


FIG. 13

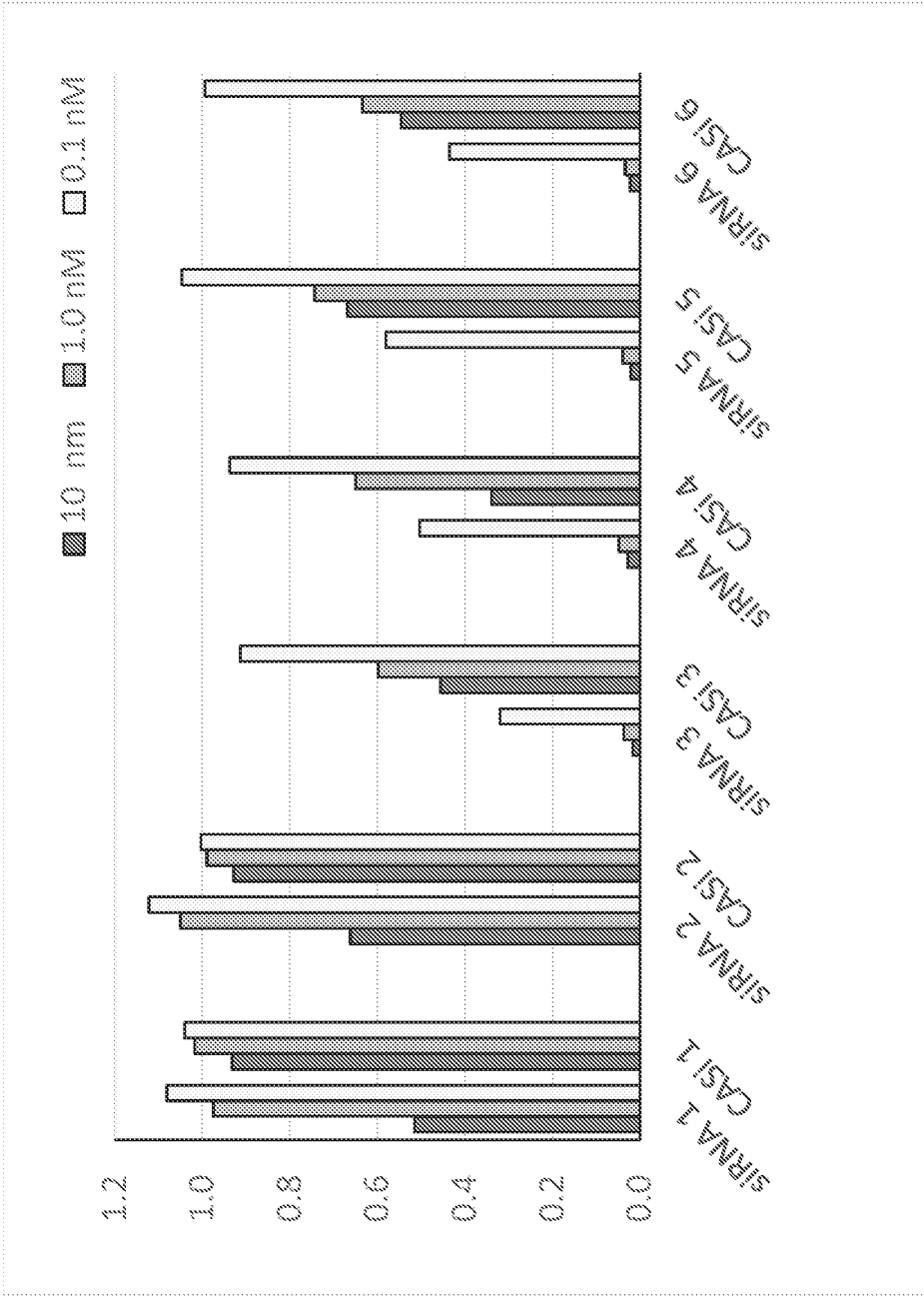


FIG. 14

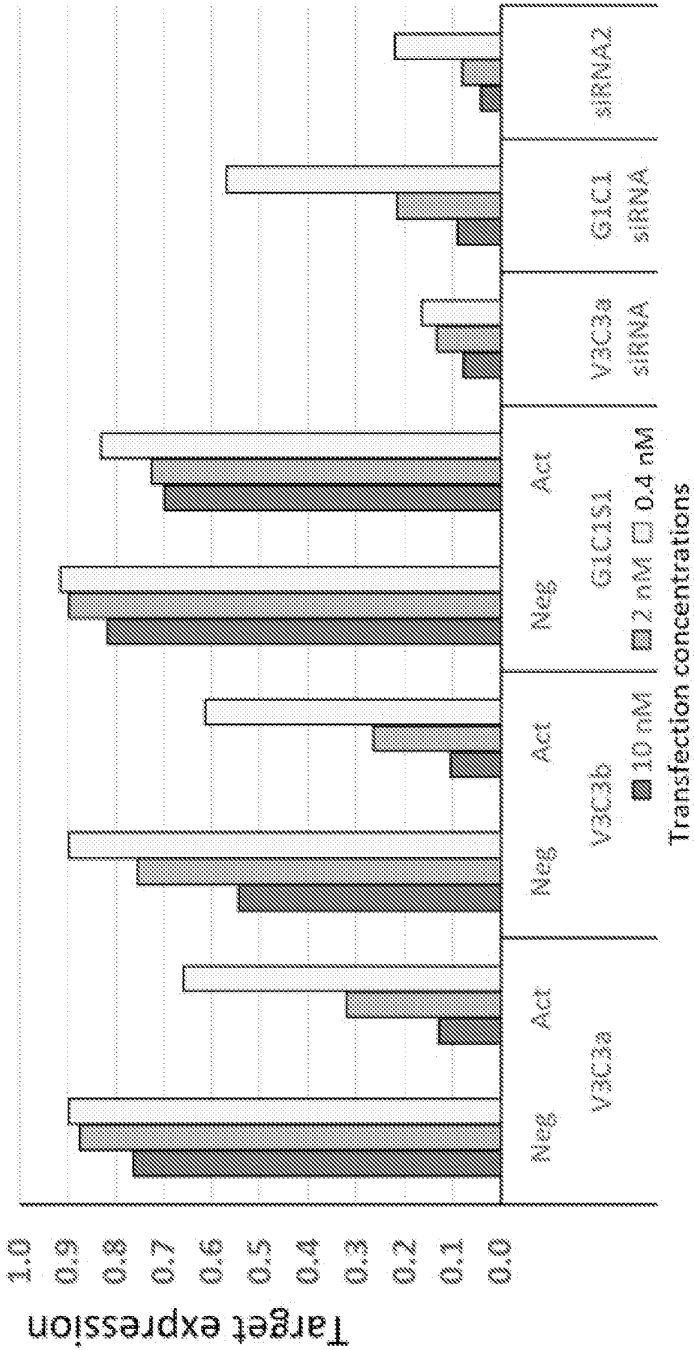


FIG. 16