

<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 1	miR-30a-5p	UGUAAACAUCCU-CGACUGGAAG
SEQ ID NO: 2	miR-30b-5p	UGUAAACAUCCU-ACACUC--AGCU
SEQ ID NO: 3	miR-30c-5p	UGUAAACAUCCU-ACACUCUCAGC
SEQ ID NO: 4	miR-30d-5p	UGUAAACAUCCC-CGACUGGAAG
SEQ ID NO: 5	miR-30e-5p	UGUAAACAUCCU-UGACUGGAAG
SEQ ID NO: 39	G007-30	UGUAAACAUCCU-CGACUGGAAG
SEQ ID NO: 38	G006-30	UGUAAACAUCCU-CGACUGGAA-
SEQ ID NO: 40	G061-30	UGUAAACAUCCC-CGACUGGAAG
SEQ ID NO: 41	G062-30	UGUAAACAUCCU-UGACUGGAAG
SEQ ID NO: 42	G063-30	UGUAAACAUCCC-UGACUGGAAG
SEQ ID NO: 43	G064-30	UGUAAACAUCCU-CACACUCUCAGC
SEQ ID NO: 44	G065-30	UGUAAACAUCCU-CACACUCUCAG-
SEQ ID NO: 45	G066-30	UGUAAACAUCCU-CACACUCUCA--

FIG. 1A

<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 6	* miR-30a-3p	CUUUCAGUC---GGAUGUUUGCAGC
SEQ ID NO: 51	P125-30	--UUCAGUC---GGAUGUUUGCAGC
SEQ ID NO: 50	P005-30	--UCCAGUC---GGAUGUUUACA--
SEQ ID NO: 48	P003-30	--UCCAGUCG-AGGAUGUUUACA--
SEQ ID NO: 49	P004-30	--UCCAGUCGCAGGAUGUUUACA--
SEQ ID NO: 47	P002-30	---CCAGUCGCAGGAUGUUUACA--
SEQ ID NO: 46	P001-30	---CCAGUCG-AGGAUGUUUACA--

*Natural

FIG. 1B

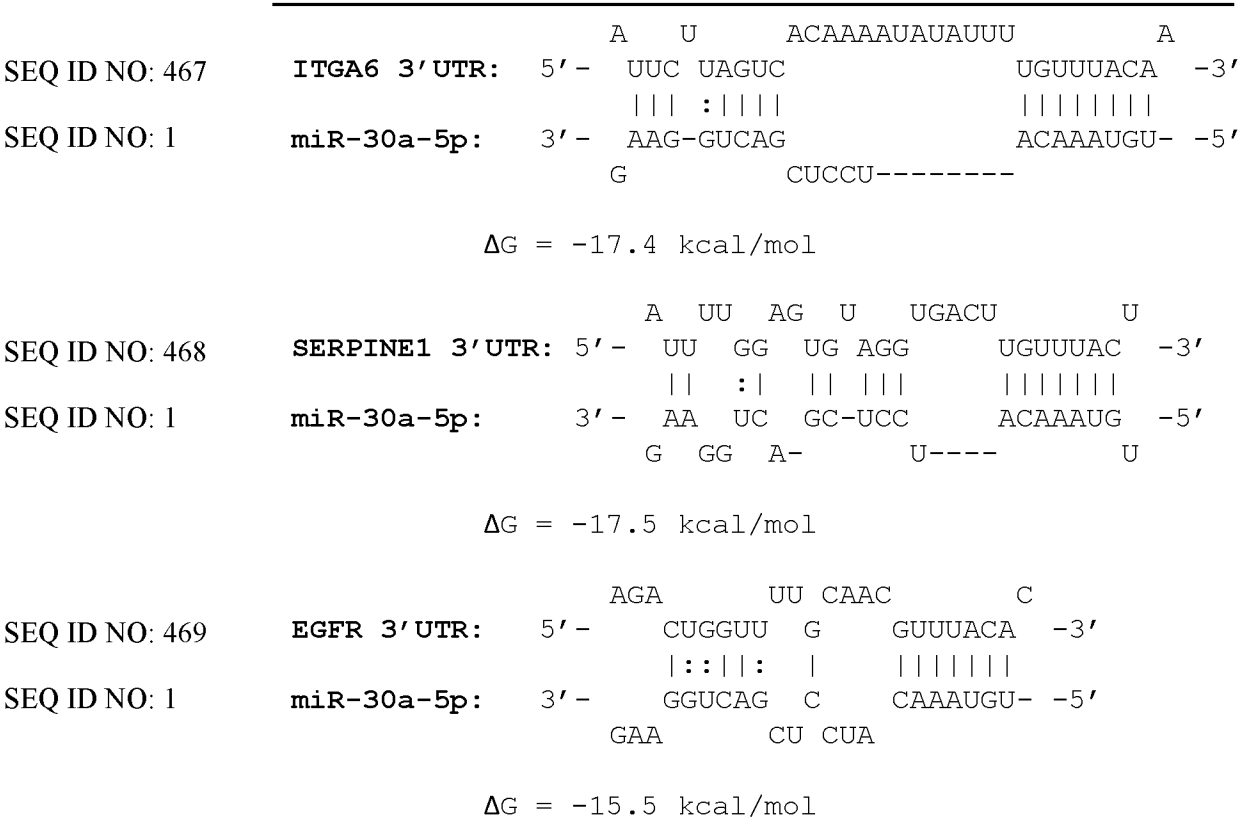


FIG. 2A

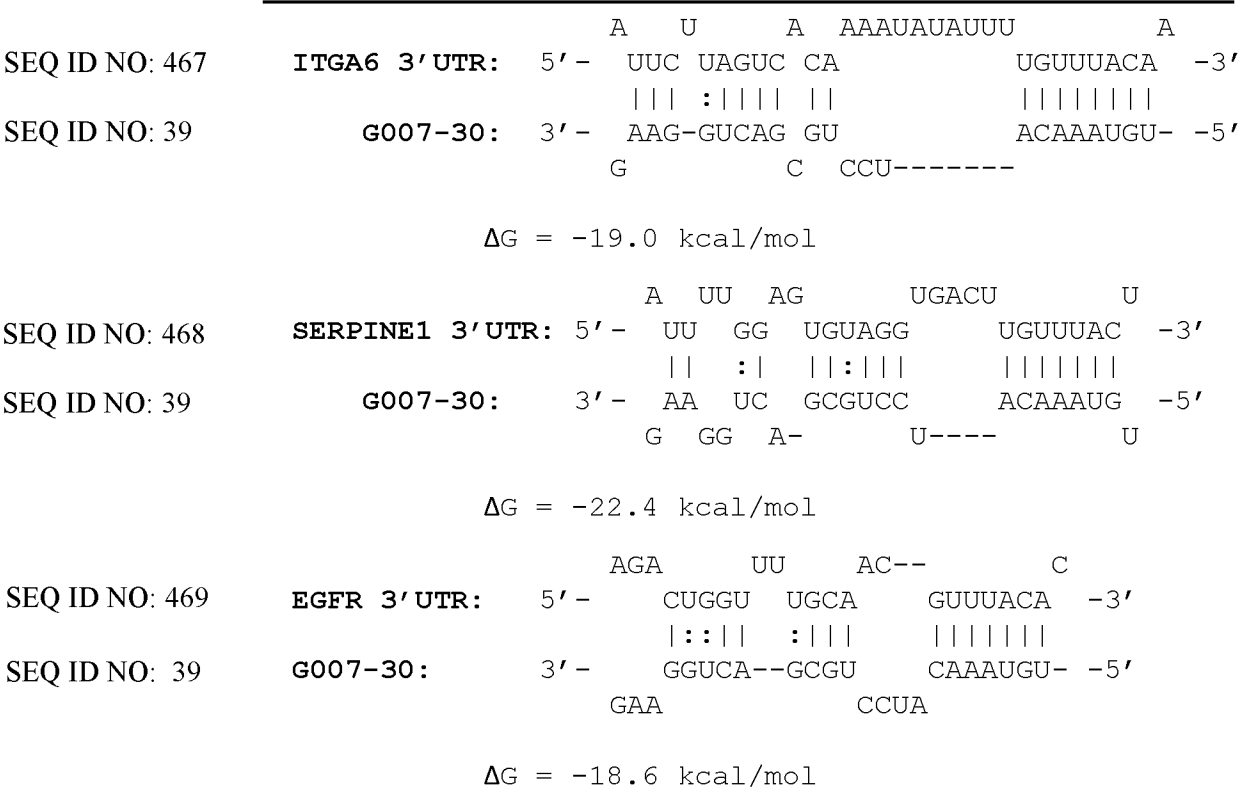


FIG. 2B

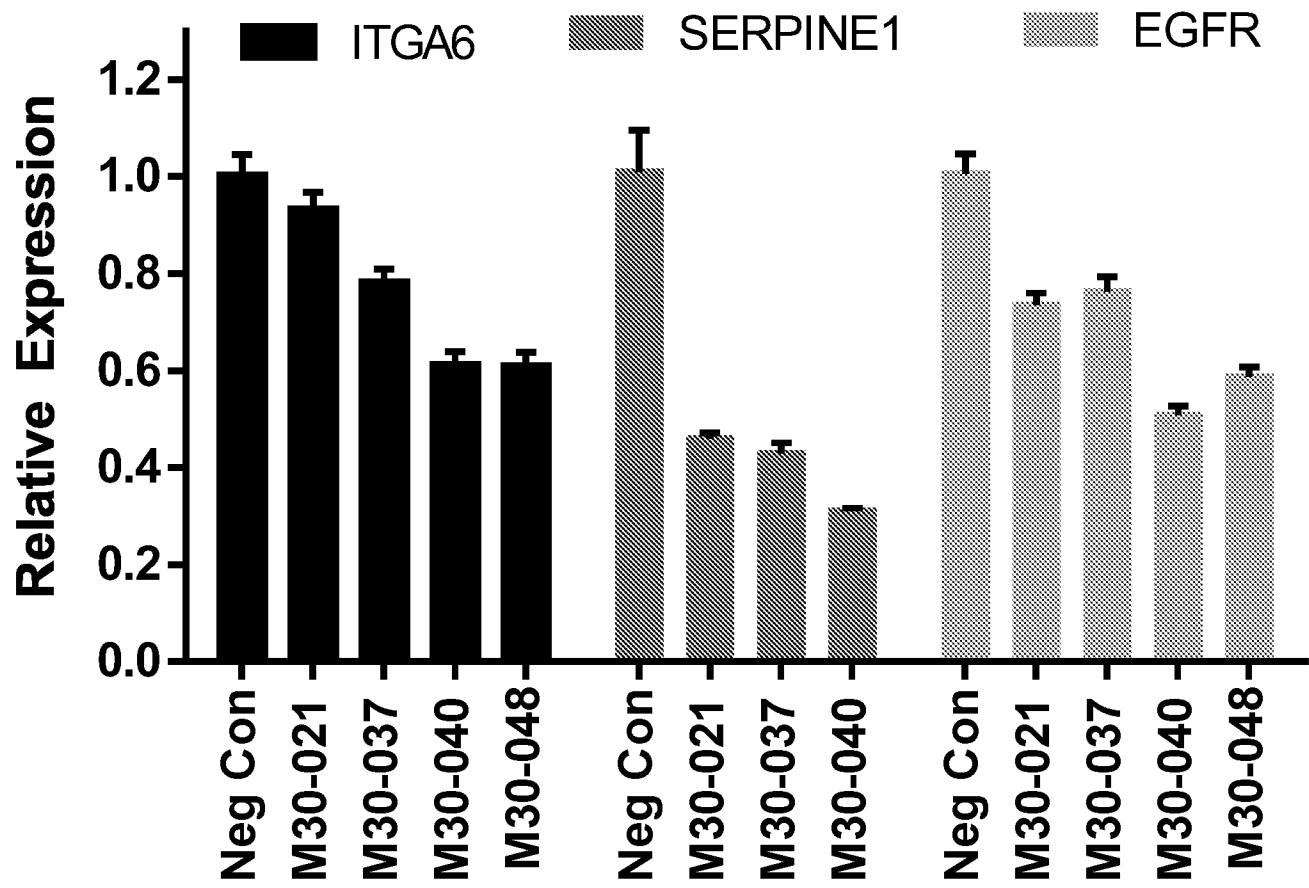
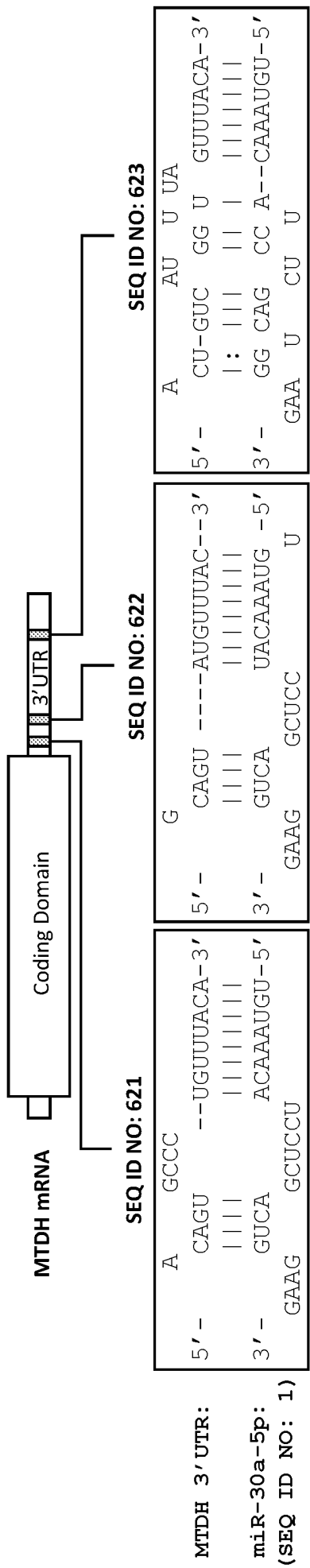


FIG. 2C



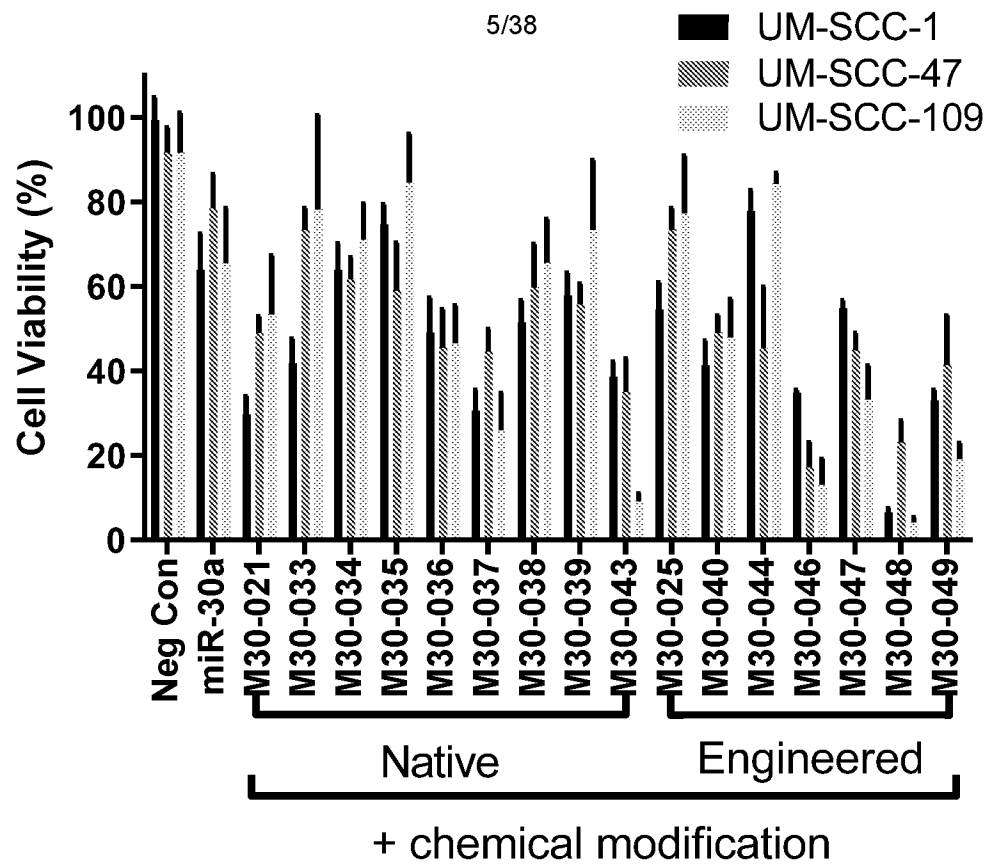


FIG. 4A

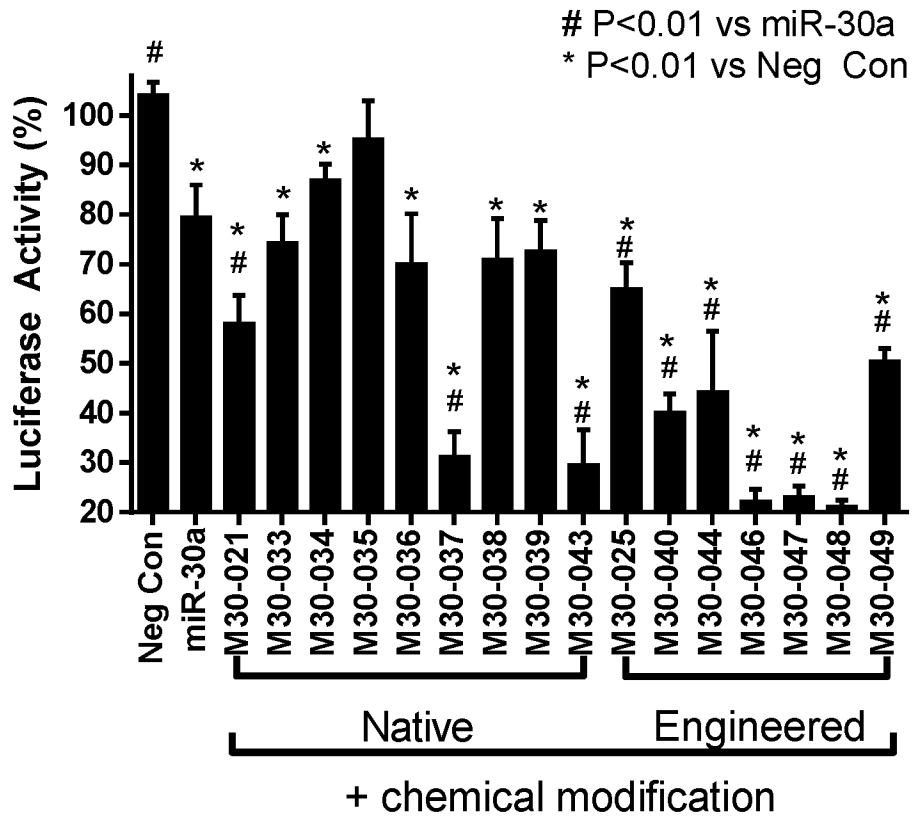


FIG. 4B

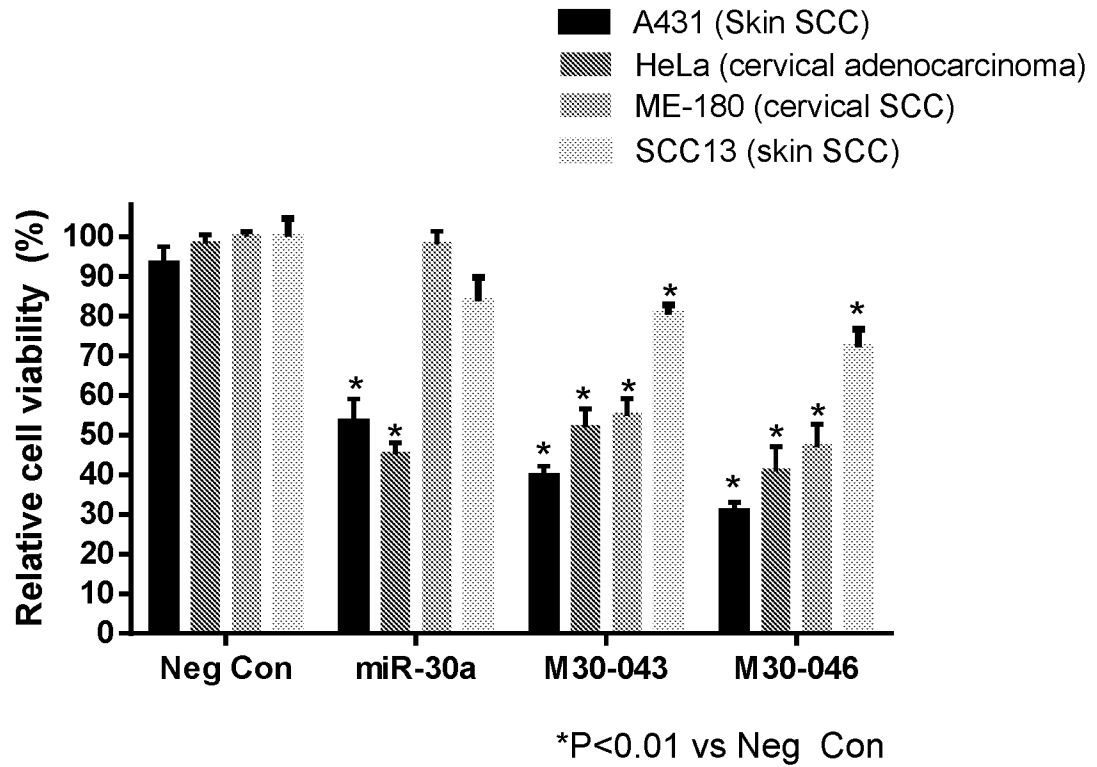


FIG. 4C

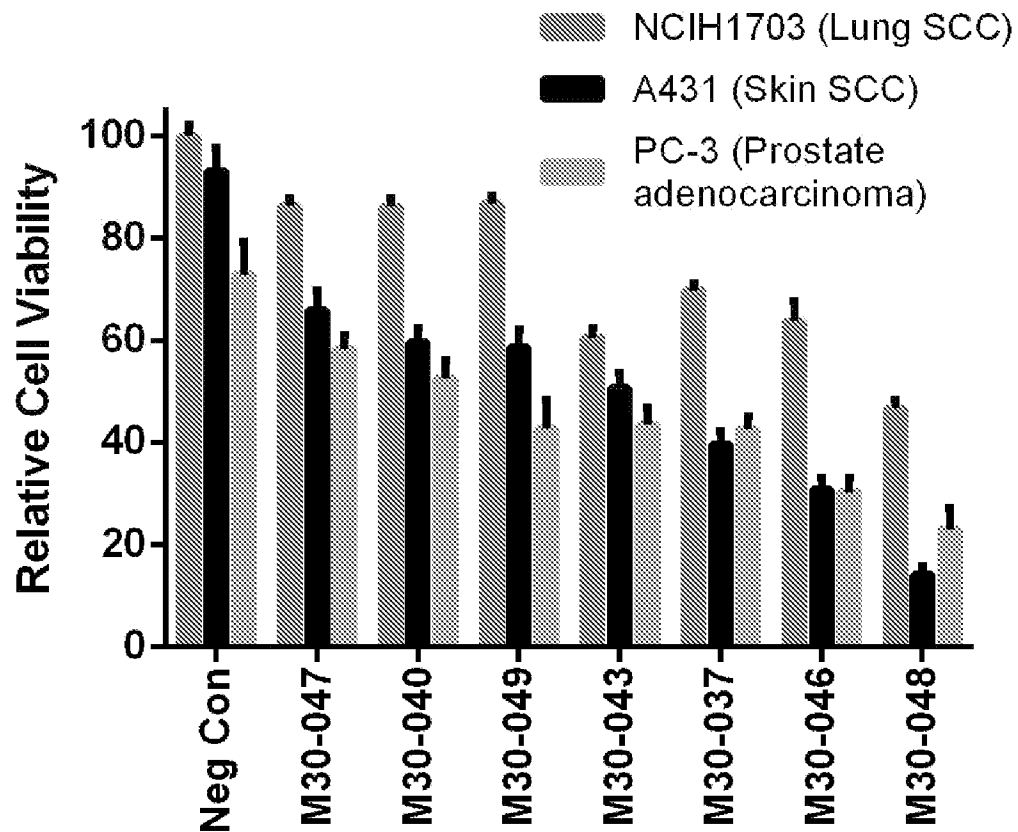


FIG. 4D

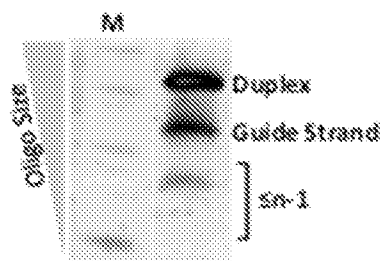


FIG. 5A

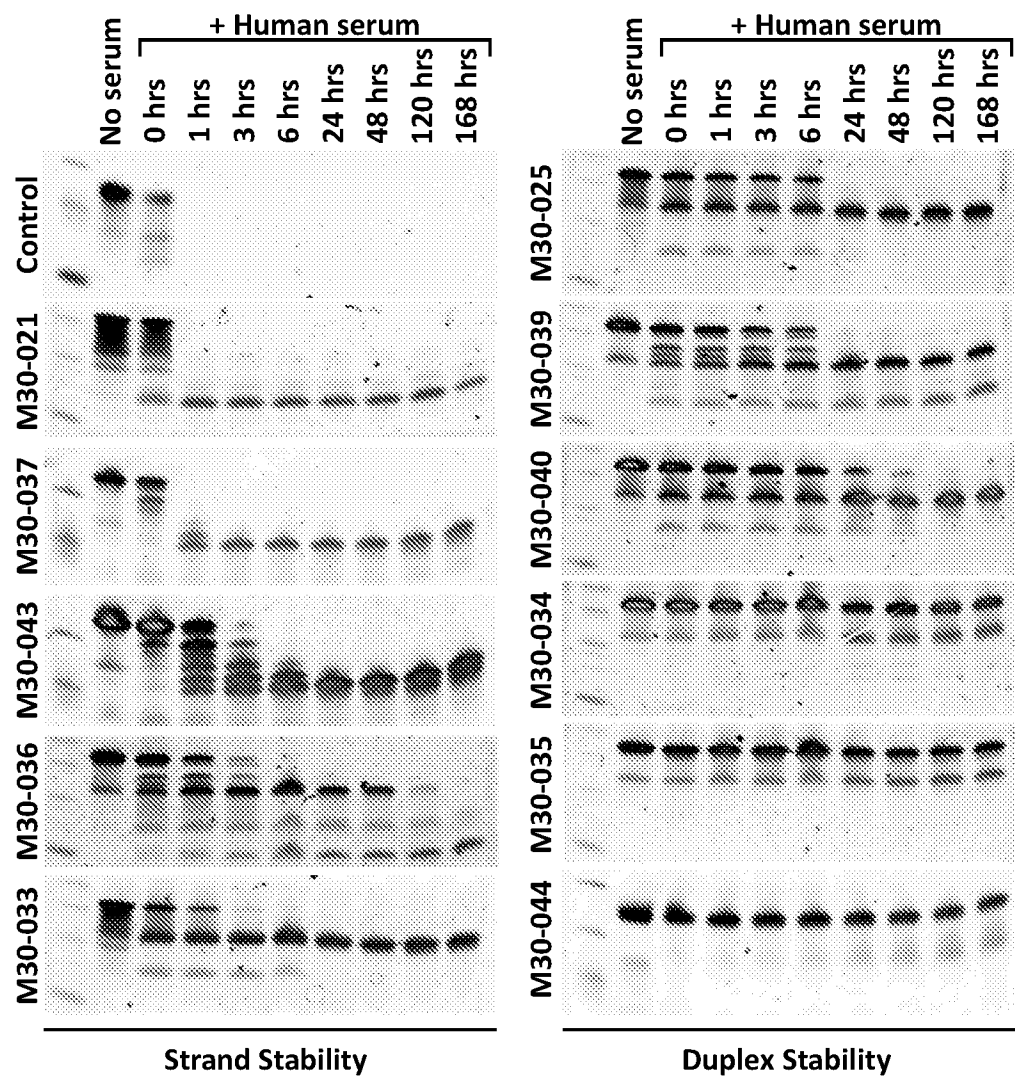


FIG. 5B

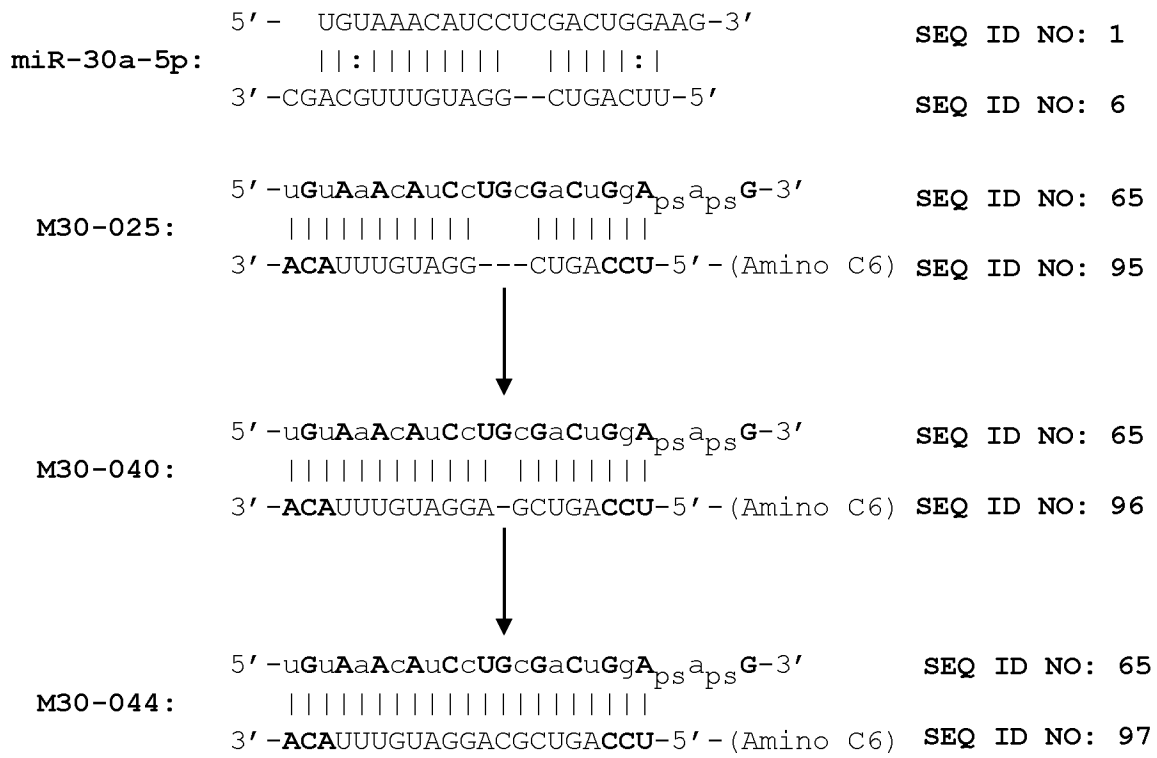


FIG. 6A

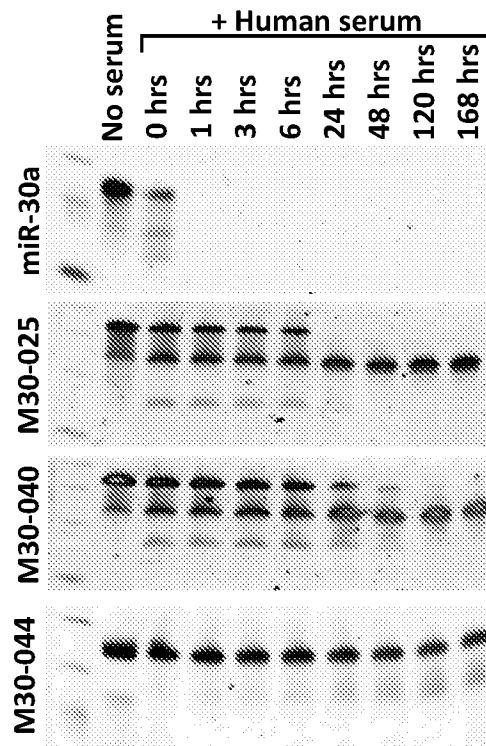


FIG. 6B

FIG. 7A

M30-033:	SEQ ID NO: 69	G042-30:	5'-UGUAAACAUC CUCGACUGGAAG-3'
M30-034:	SEQ ID NO: 95	P014-30:	3'-ACAUUUGUAGG--CUGACCU-5'
M30-034:	SEQ ID NO: 69	G042-30:	5'-UGUAAACAUC CUCGACUGGAAG-3'
M30-040:	SEQ ID NO: 96	P123-30:	3'-ACAUUUGUAGGAGCUGACCU-5'
M30-040:	SEQ ID NO: 65	G032-30:	5'-UGUAAACAUC CUCGACUGGAAG-3'
M30-040:	SEQ ID NO: 96	P123-30:	3'-ACAUUUGUAGGA-GCUGACCU-5'

FIG. 7B

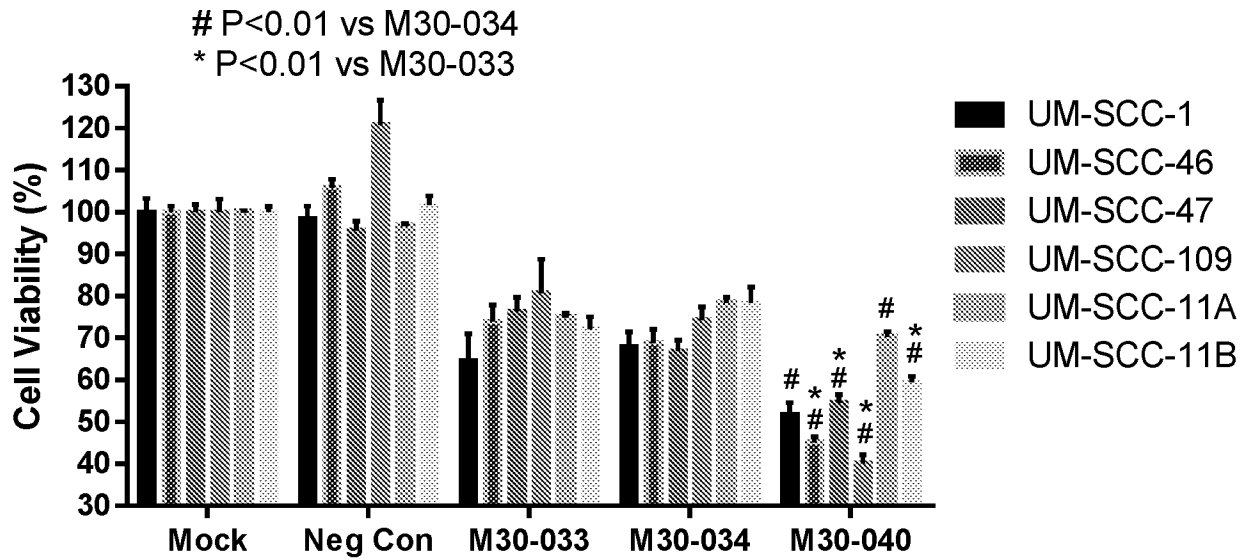
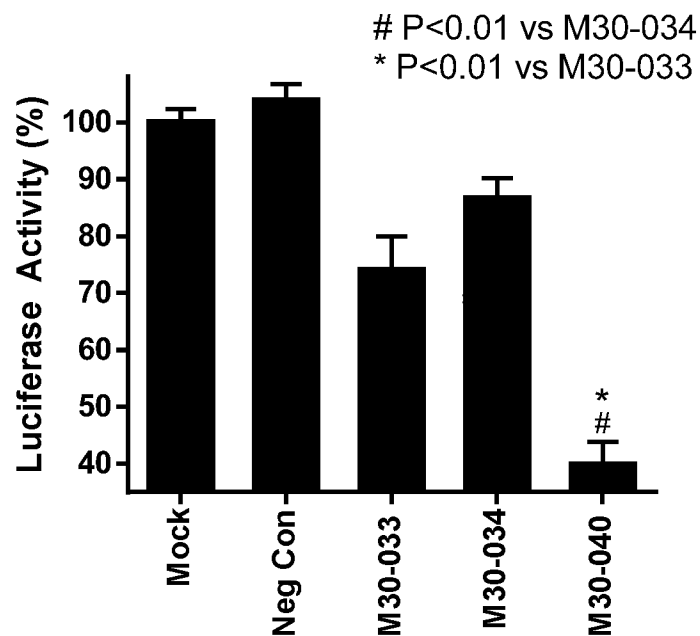
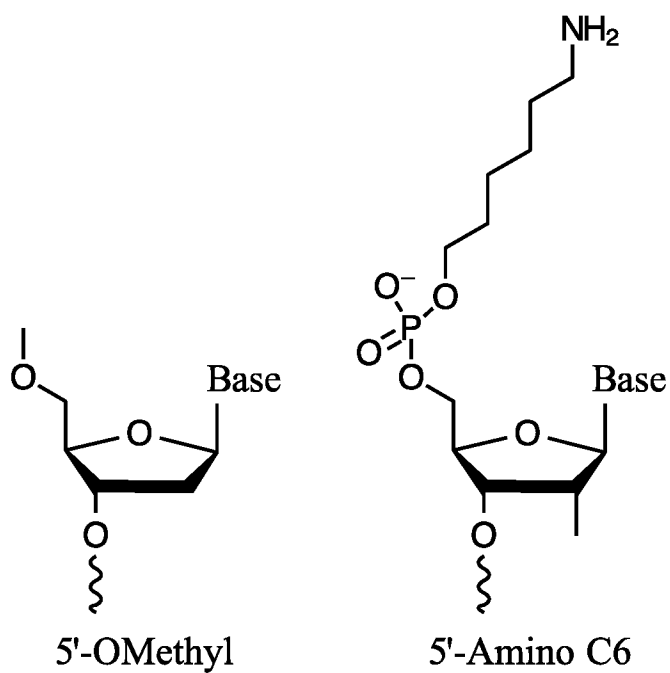
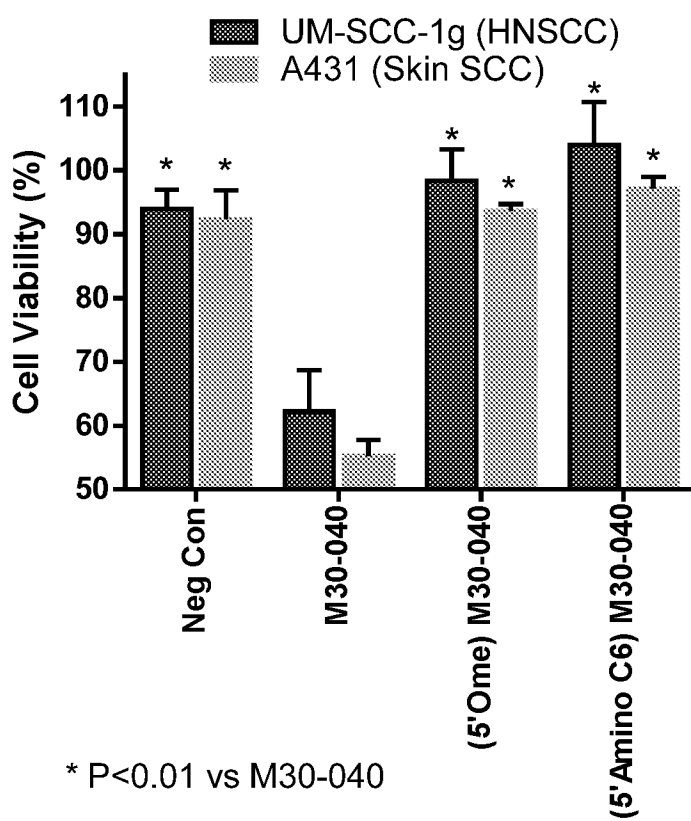


FIG. 7C



**FIG. 8A****FIG. 8B**

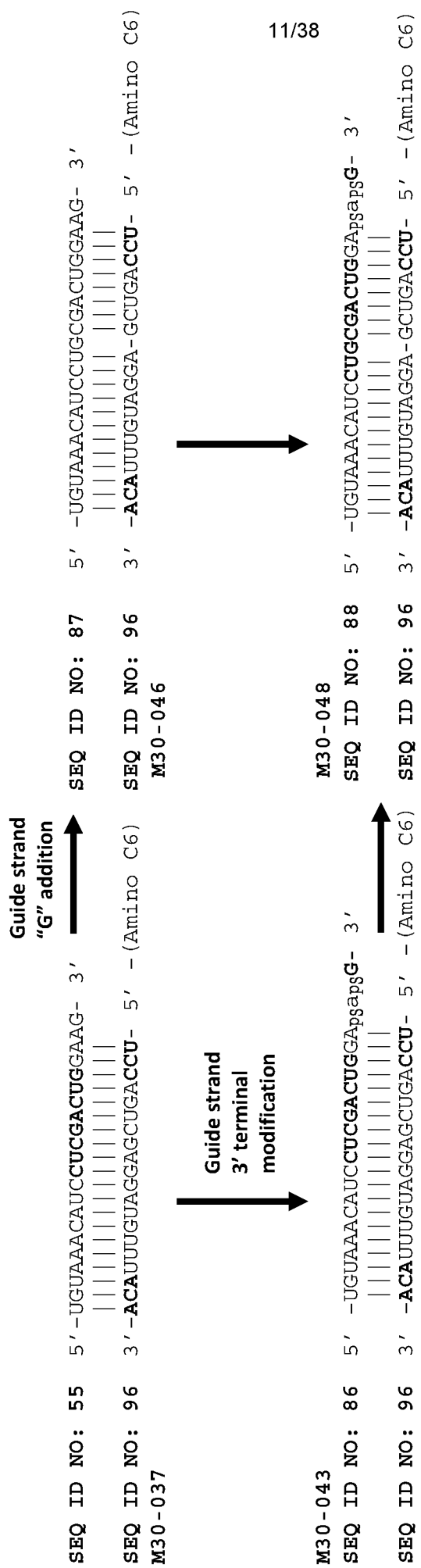


FIG. 9A

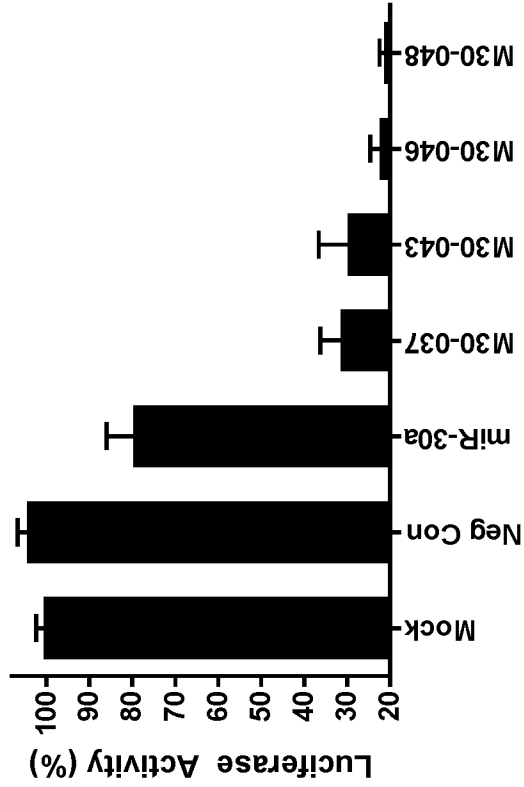


FIG. 9C

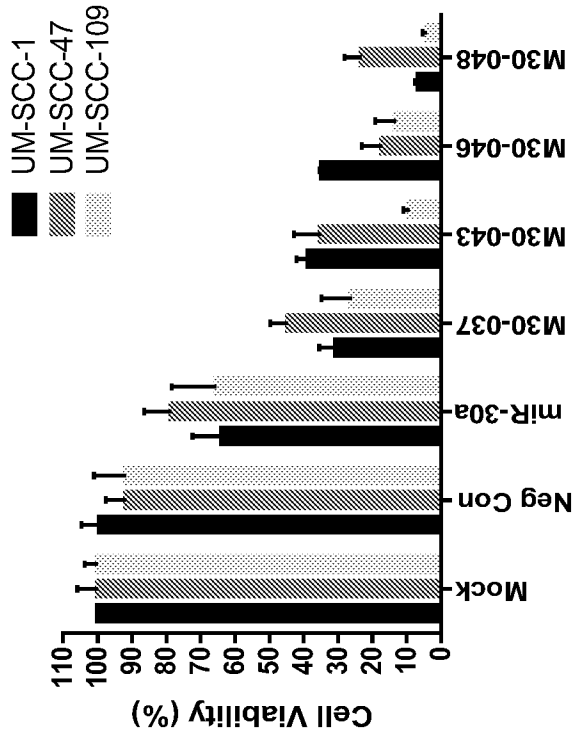


FIG. 9B

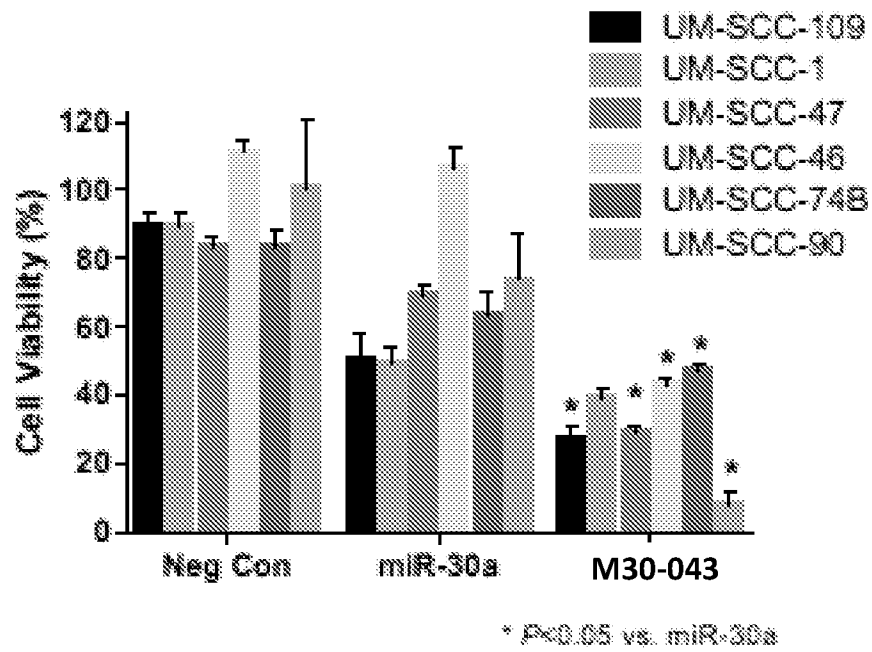


FIG. 10A

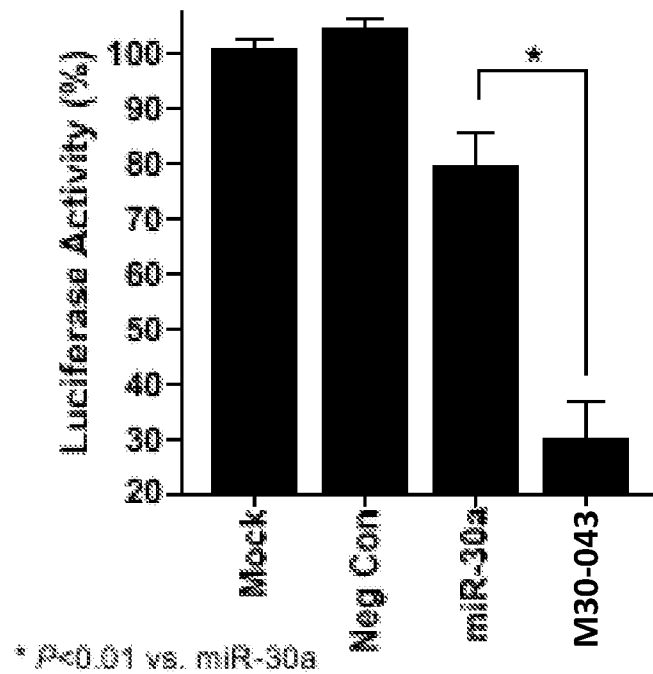


FIG. 10B

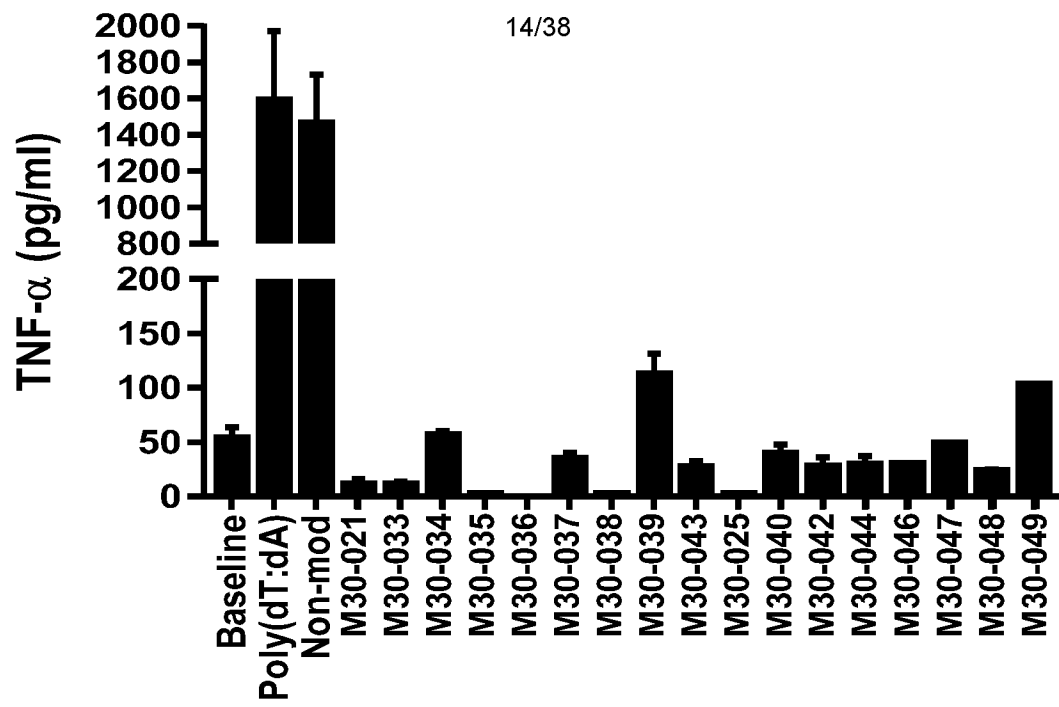


FIG. 11A

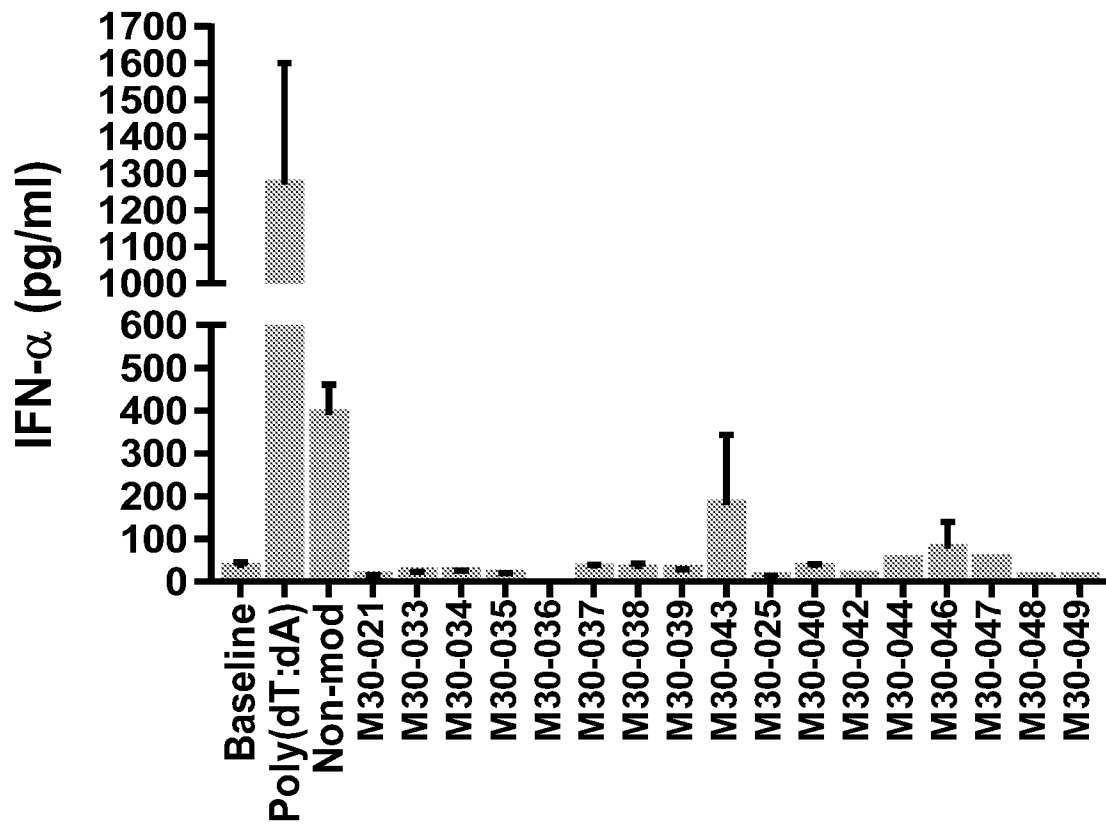


FIG. 11B

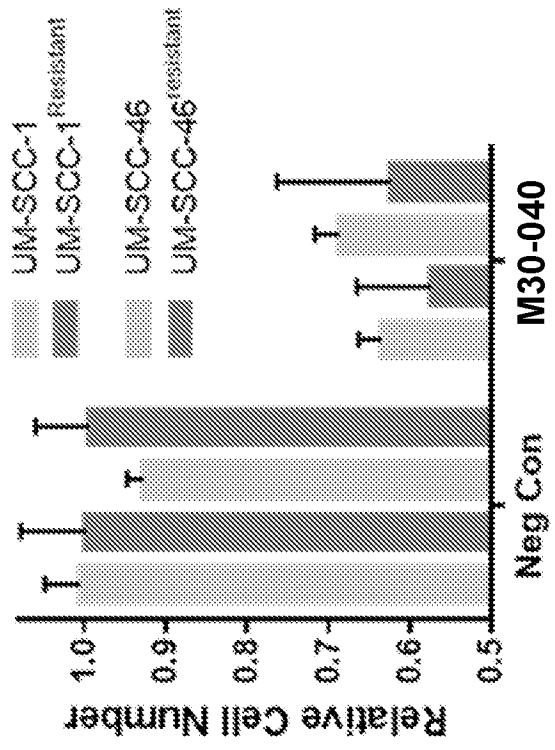


FIG. 12B

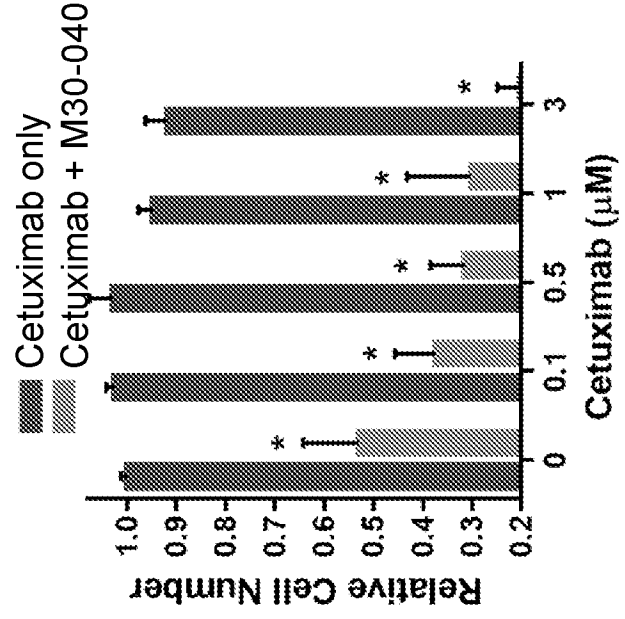


FIG. 12D

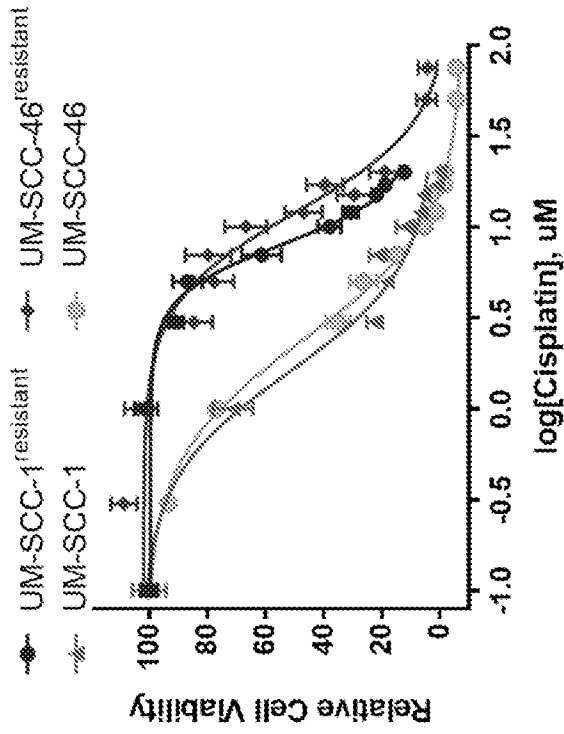


FIG. 12A

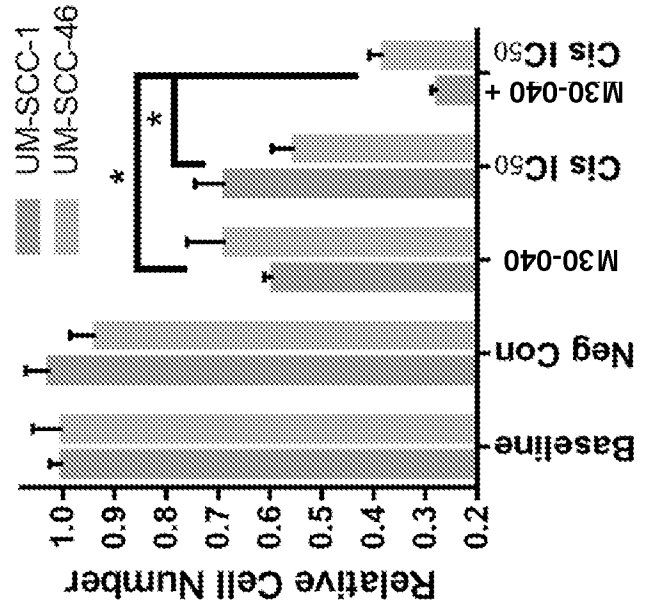
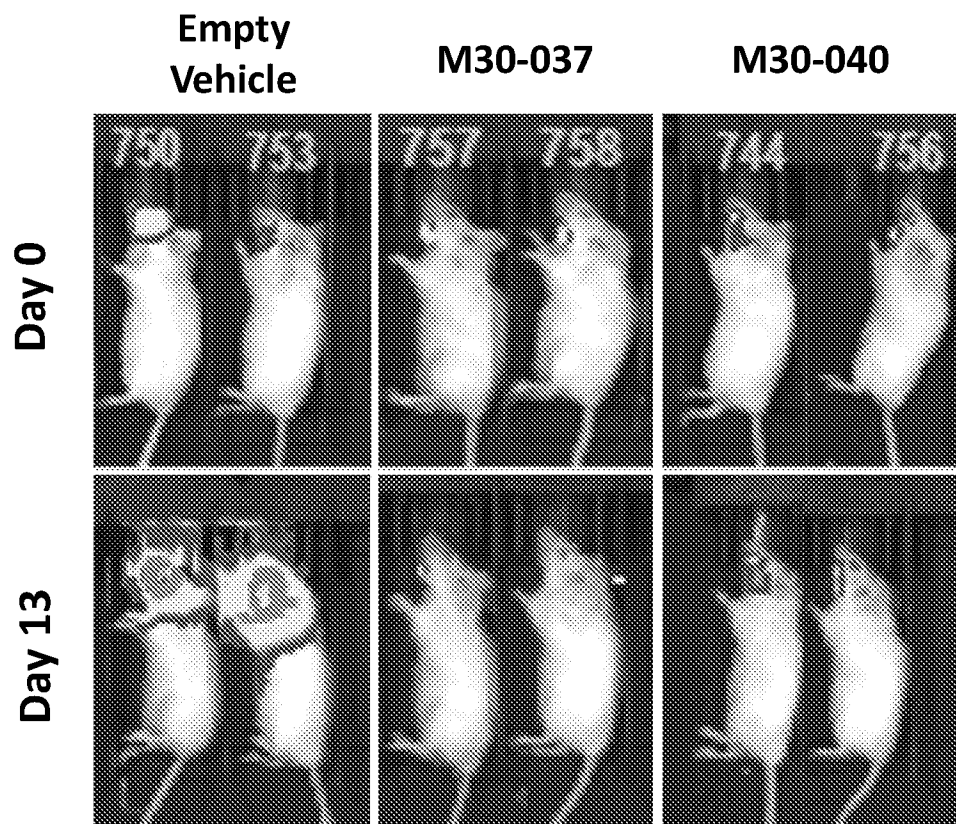
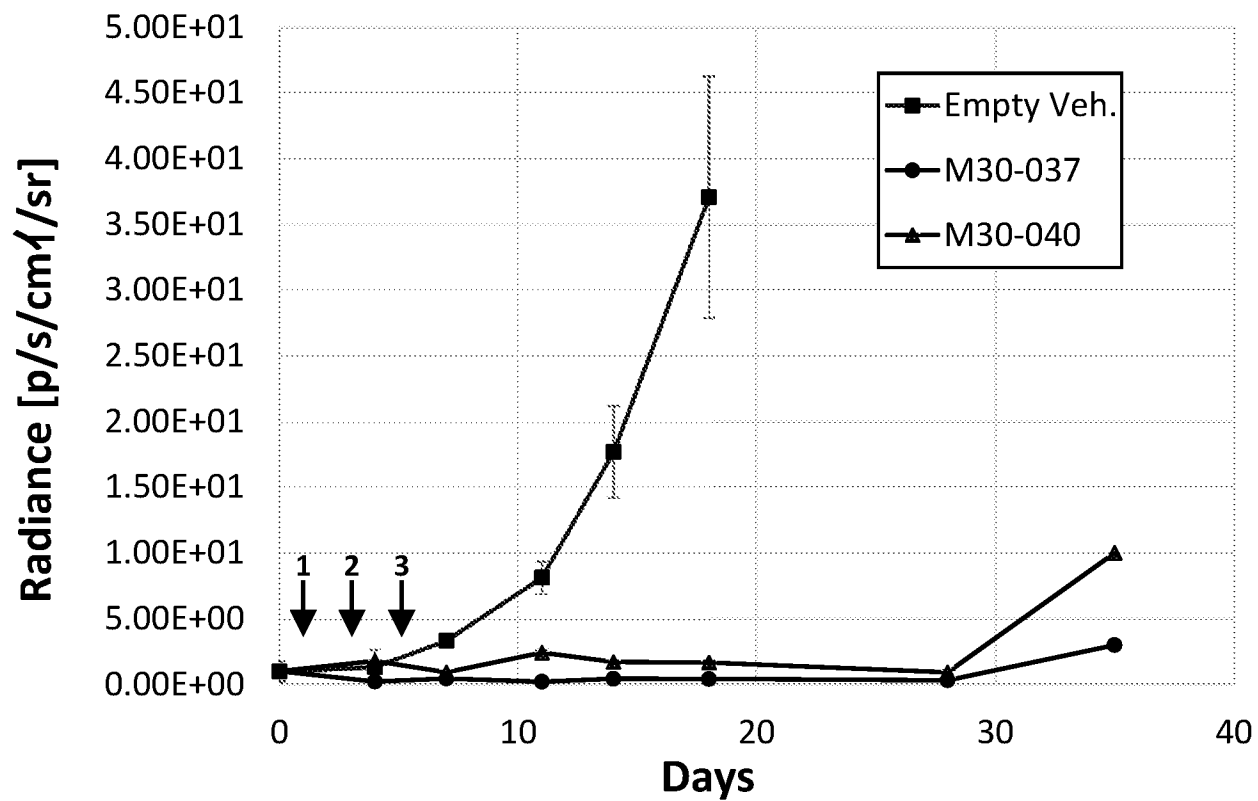
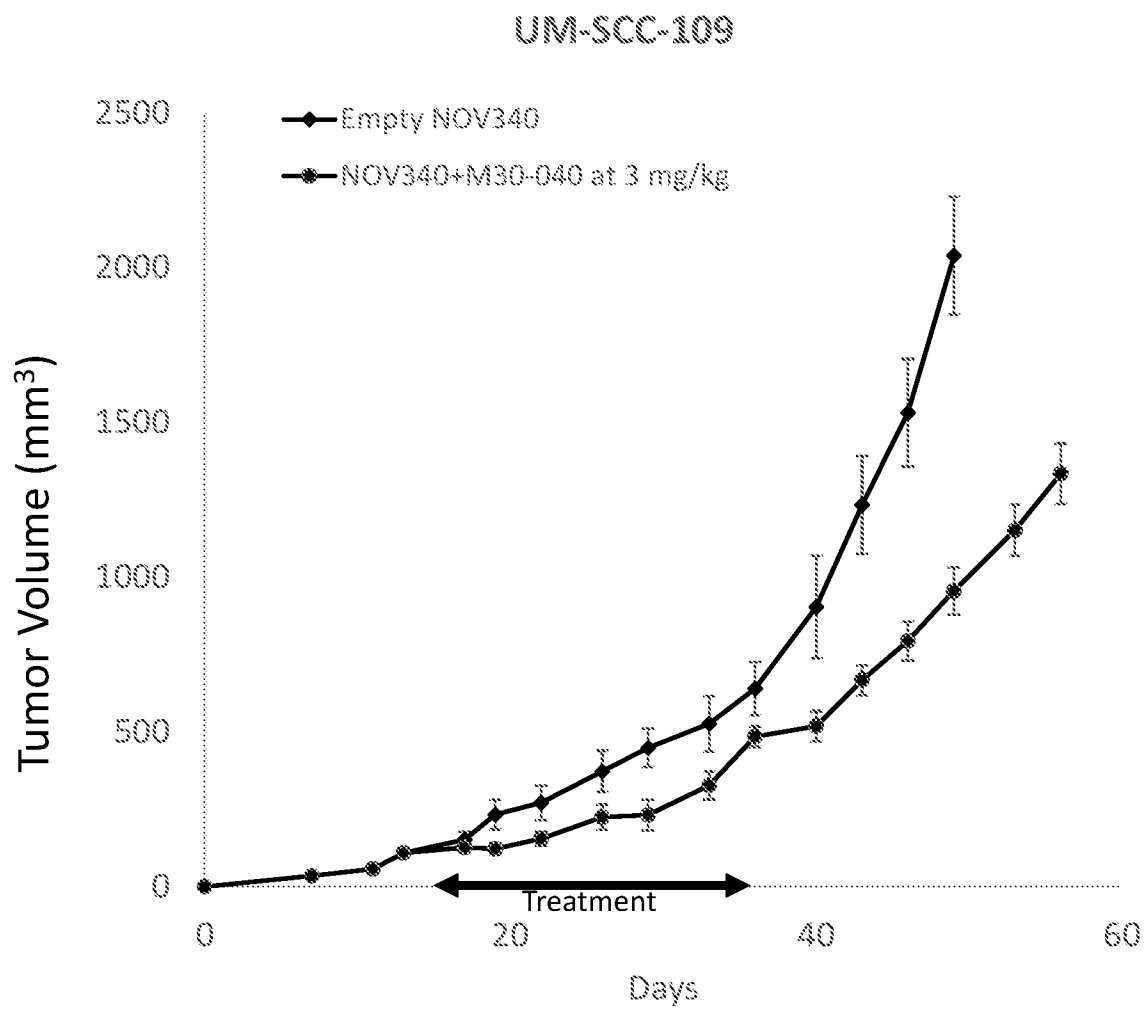


FIG. 12C

**FIG. 13A****FIG. 13B**

**FIG. 13C**

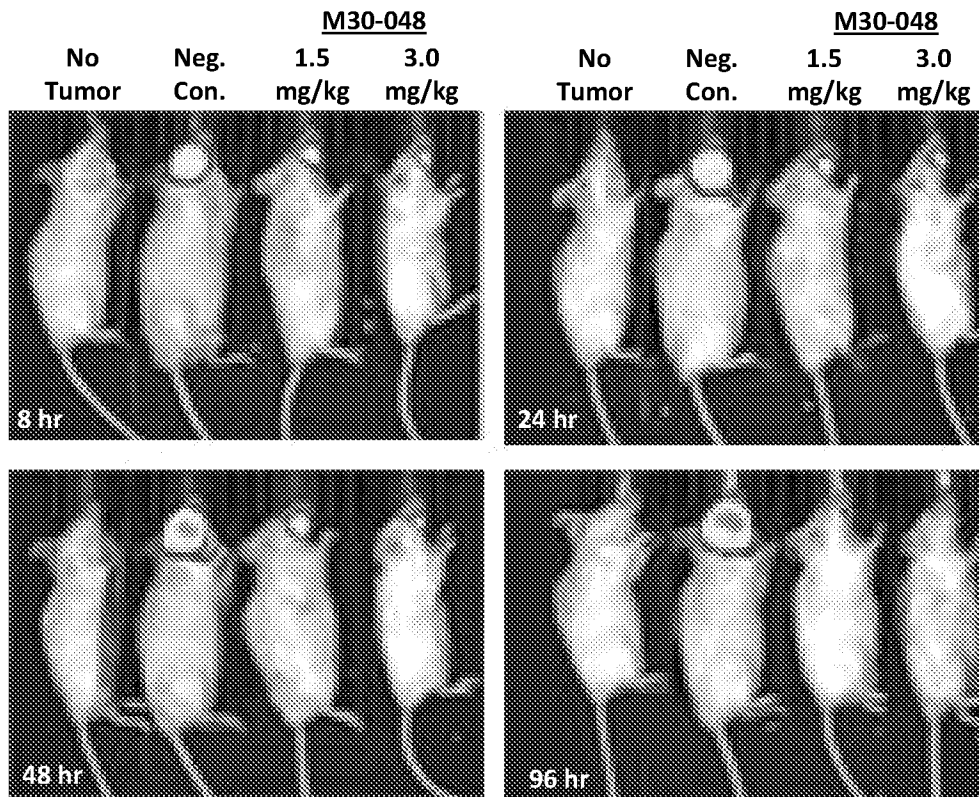


FIG. 14A

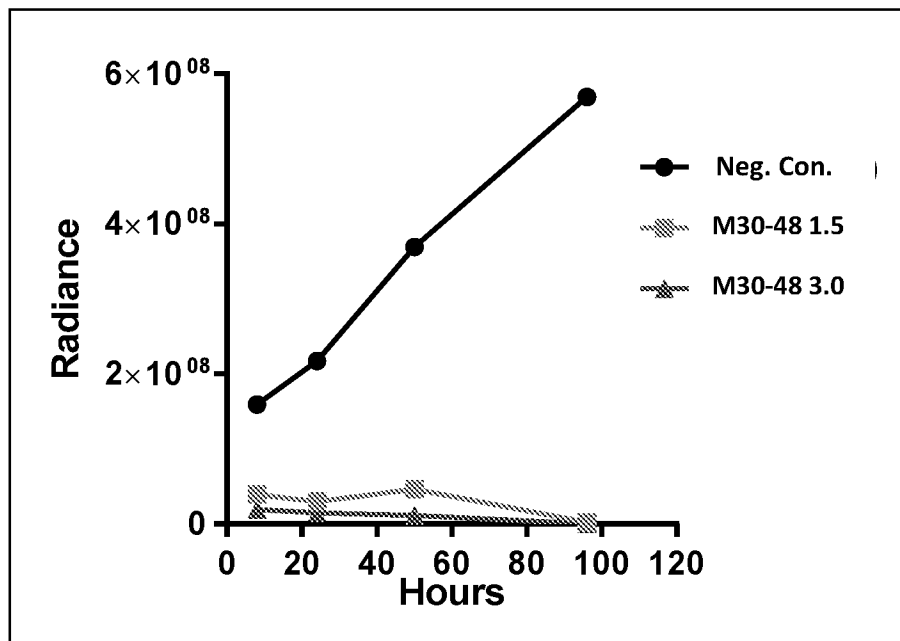


FIG. 14B

<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 12	Natural	miR-29a-3p UAGCACCAUUGAAAUCGGUUA
SEQ ID NO: 13		miR-29b-3p UAGCACCAUUUGAAAUCAGUGUU
SEQ ID NO: 14		miR-29c-3p UAGCACCAUUUGAAAUCGGUUA
SEQ ID NO: 102	Engineered	G003-29 UAGCACCAUUGAAAUCAGUGUU
SEQ ID NO: 101		G002-29 UAGCACCAUUGAAAUCAGUGU-
SEQ ID NO: 103		G004-29 UAGCACCAUUUGAAGUCAGUGUU
SEQ ID NO: 118		G028-29 UAGCACCAUUUGAAGUCAGUGU-
SEQ ID NO: 112		G022-29 UAGCACCAUUUGAAAGCAGUGUU
SEQ ID NO: 111		G021-29 UAGCACCAUUUGAAAGCAGUGU-
SEQ ID NO: 115		G025-29 UAGCACCAUUUGAAGGCAGUGU-
SEQ ID NO: 119		G029-29 UAGCACCAUUUGAAAGUCAGUGUU
SEQ ID NO: 120		G030-29 UAGCACCAUUUGAAAGUCAGUG--
SEQ ID NO: 117		G027-29 UAGCACCAUUUGAAGGUCAGUGUU
SEQ ID NO: 116		G026-29 UAGCACCAUUUGAAGGUCAGUG--
SEQ ID NO: 105		G006-29 UAGCACCAUUGAAGUCAGUGUU
SEQ ID NO: 110		G020-29 UAGCACCAUUGAAGGUCAGUGUU
SEQ ID NO: 109		G019-29 UAGCACCAUUGAAGGCAGUGUU
SEQ ID NO: 100		G001-29 UAGCACCAUUGAAAGCAGUGUU

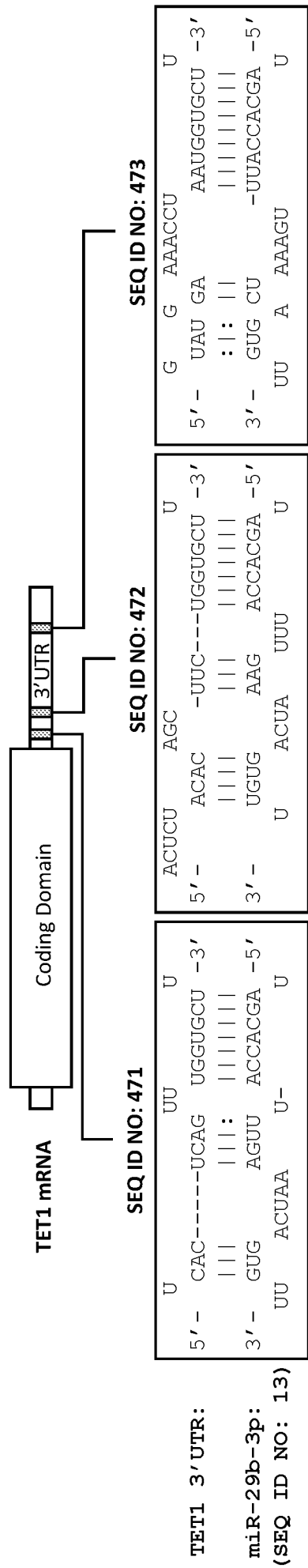
Hybrid

Mutation

Insert.

Mut. +
Insert.Hybrid
+ Mut.
+insert.

FIG. 15



SEQ ID NO:	Strand	SEQ ID NO:			471	472	373	NET	Avg
13	miR-29b-3p				-18.9	-19.2	-18.4	-56.5	-18.83
102	G003-29				-21.1	-19.2	-17	-57.3	-19.1
103	G004-29				-18.9	-24	-19.3	-62.2	-20.73
112	G022-29				-18.9	-23.7	-17.9	-60.5	-20.17
115	G025-29				-19.2	-23.6	-20.6	-63.4	-21.13
119	G029-29				-19	-20.2	-19.7	-58.9	-19.63
117	G027-29				-19.3	-22.7	-22.3	-64.3	-21.43
105	G006-29				-21.1	-24	-17.8	-62.9	-20.97
110	G020-29				-21.5	-22.7	-20.5	-64.7	-21.57
109	G019-29				-21.1	-23.7	-18.7	-63.5	-21.17
100	G001-29				-21.1	-23.7	-17	-61.8	-20.6

Hybridization Free Energy (kcal/mol)

FIG. 16

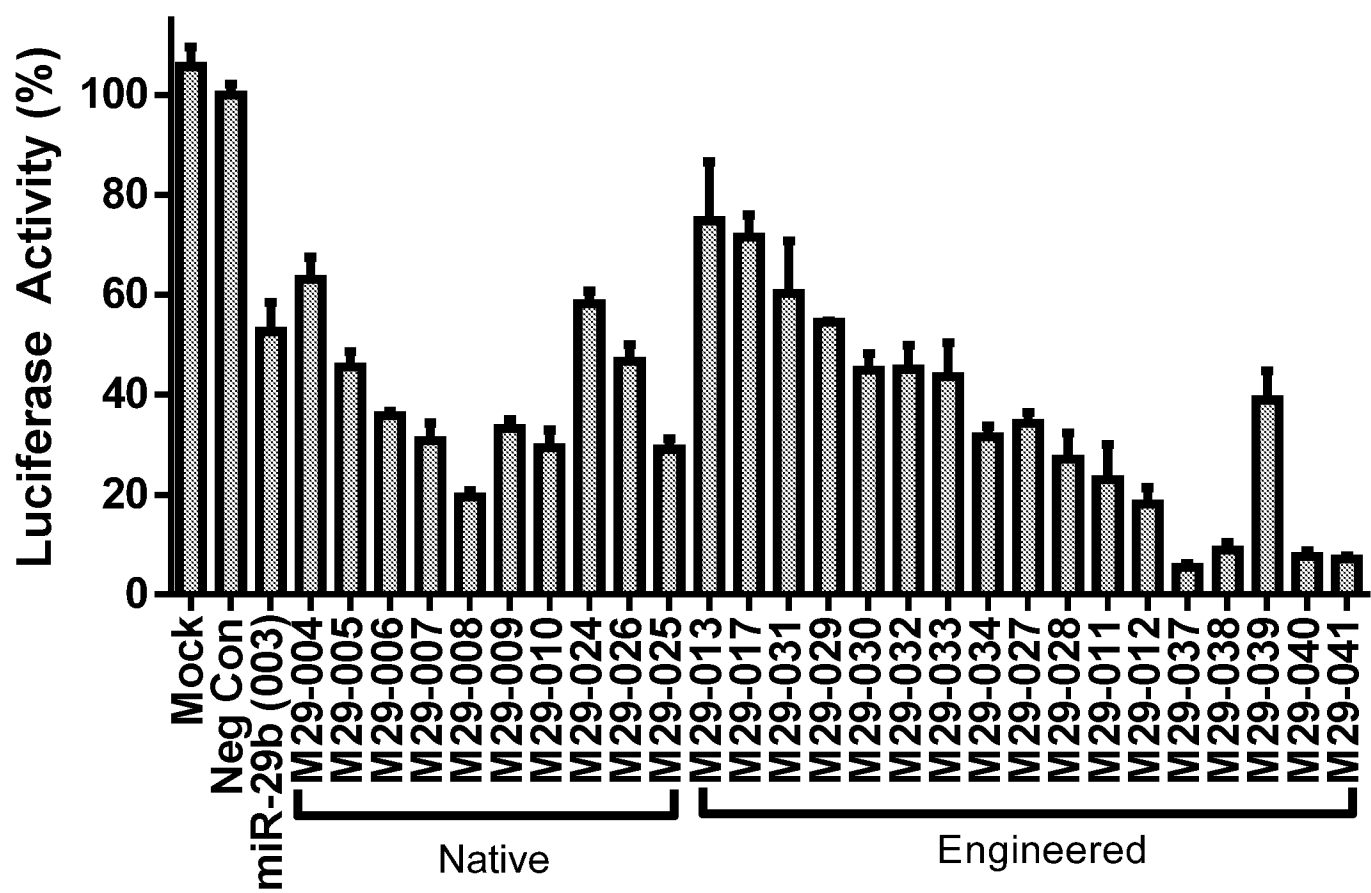


FIG. 17

	No serum	+ Human serum							
		0 min	1 min	5 min	15 min	30 min	1 hr	2 hr	4 hr
miR-29b-1									
M29-004									
M29-012									

FIG. 18B

M29-024:	(Amino C6)-5'-ACUGAUUUCAGAUGGUGUUA-3'	SEQ ID NO:173
	: :	
	3'-UuGuGaCuAaAgUuUaCcAcGaU-5'	SEQ ID NO:127
M29-026:	(Amino C6)-5'-GCUGGUUUCAGAUGGUG UUA-3'	SEQ ID NO:171
	: : : :	
	3'-UuGuGaCuAaAgUuUaCcAc GaU-5'	SEQ ID NO:127
M29-028:	(Amino C6)-5'-CACUGAUUUCAGAUGGUGUUA-3'	SEQ ID NO:176
	: :	
	3'-UuGuGaCuAaAqUcUaCcAcGaU-5'	SEQ ID NO:128

FIG. 19A

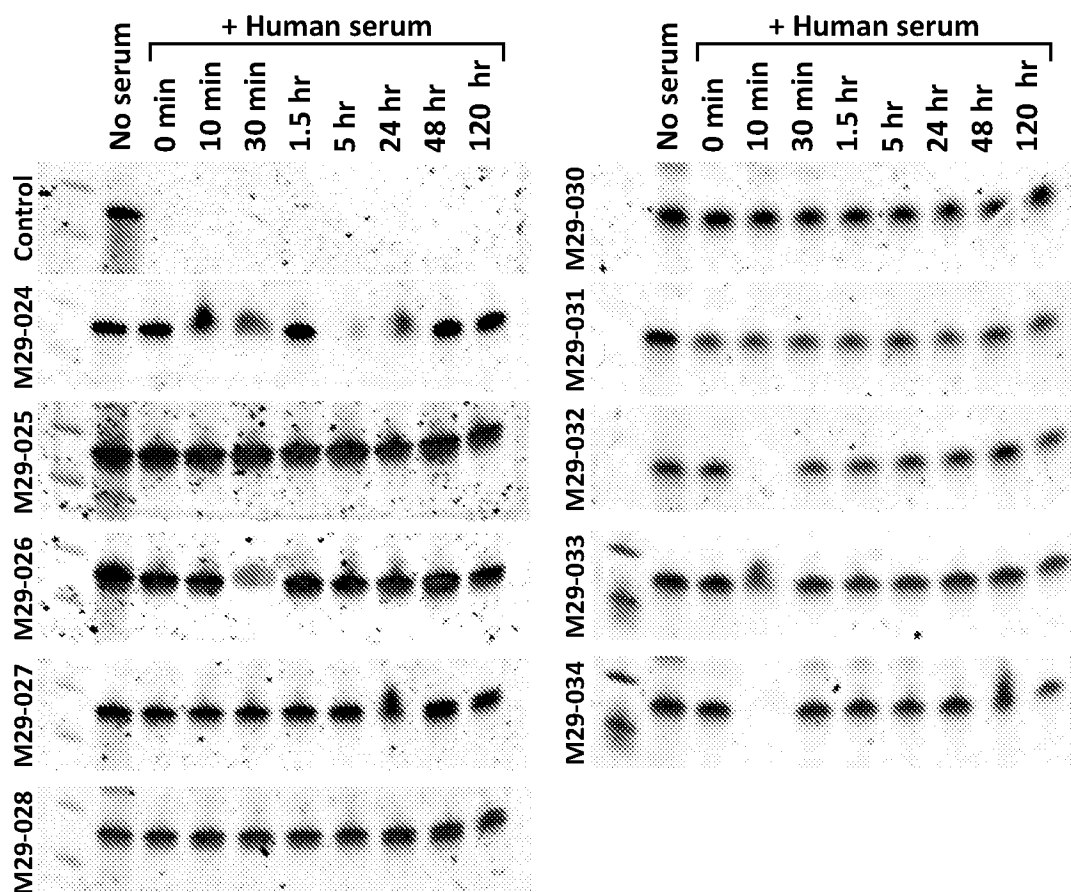


FIG. 19B

UUU
 5' - ACUGAUUUC UGGUGUUAG-3' miR-29a-5p SEQ ID NO: 15
 ||:||||| ||||:|
 3' -AUUGGCUAAAG ACCACGAU -5' miR-29a-3p SEQ ID NO: 12
 UCU

UUU
 (Amino C6)-5' - ACCGAUUUC UGGUGUUA-3' P010-29 SEQ ID NO: 158
 M29-023 ||||| ||||:|
 3' -AUUGGCUAAAG ACCACGAU-5' miR-29a-3p SEQ ID NO: 12
 UCU

(Amino C6)-5' - ACCGAUUUCAGAU GGUGUUA-3' P009-29 SEQ ID NO: 175
 M29-002 ||||| ||||:|
 3' -AUUGGCUAAAGUCUACCACGAU-5' miR-29a-3p SEQ ID NO: 12

FIG. 20A

U GU
 5' - GCUGGUUUC AUGGUG UUAGA-3' miR-29b-1-5p SEQ ID NO: 16
 :|||:|||| ||||| :||
 3' -UUGUGACUAAAGU UACCAC GAU -5' miR-29b-3p SEQ ID NO: 13
 U --

(Amino C6)-5' - ACUGAUUUCAGAU GGUGUUA-3' P007-29 SEQ ID NO: 173
 M29-007 ||||| ||||:|||||:|
 3' -UUGUGACUAAAGUUUACCACGAU-5' miR-29b-3p SEQ ID NO: 13

(Amino C6)-5' - CACUGAUUUCAGAU GGUGUUA-3' P011-29 SEQ ID NO: 176
 M29-008 ||||| ||||:|||||:|
 3' -UUGUGACUAAAGUUUACCACGAU-5' miR-29b-3p SEQ ID NO: 13

FIG. 20B

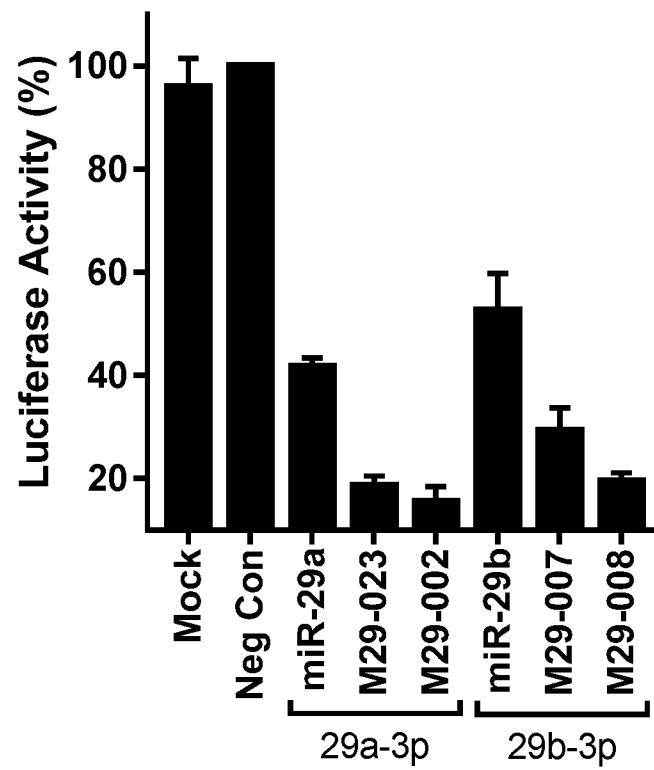


FIG. 20C

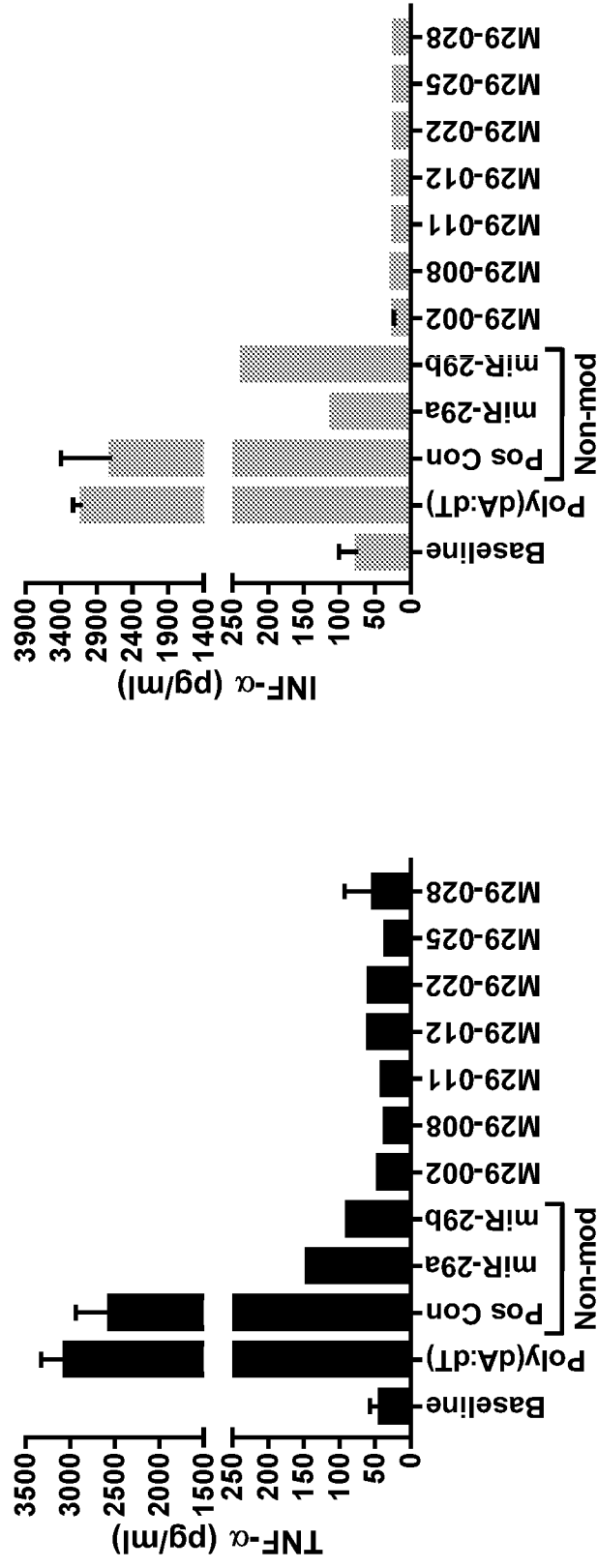


FIG. 21

<hr/>				
	UC	CC		
HIV-1 NEF site:	5'-	CACUGA	UUUGGAUGGUGCUA -3'	SEQ ID NO: 470
			:::	
miR-29b-3p:	3'-	GUGACU	-AAGUUUACCCACGAU -5'	SEQ ID NO: 13
	UU	A		
	$\Delta G = -29.9 \text{ kcal/mol}$			
<hr/>				
	UC	C		
HIV-1 NEF site:	5'-	CACUGA	CUUUGGAUGGUGCUA -3'	SEQ ID NO: 470
			:::	
G004-29:	3'-	GUGACU	-GAAGUUUACCCACGAU -5'	SEQ ID NO: 103
	UU			
	$\Delta G = -33.6 \text{ kcal/mol}$			
<hr/>				
	UC			
HIV-1 NEF site:	5'-	CACUGACCUUUGGAUGGUGCUA -3'	SEQ ID NO: 470	
			:::	
G027-29:	3'-	GUGACUGGAAGUUUACCCACGAU -5'	SEQ ID NO: 117	
	UU			
	$\Delta G = -40.6 \text{ kcal/mol}$			
<hr/>				

FIG. 22A

UC		CC	
HIV-1 NEF site:	5' -	CACUGA	UUUGGAUGGUGCUA -3'
			::
G003-29:	3' -	GUGACU	-AAGUCUACACGAU -5'
		UU	A
$\Delta G = -32.6 \text{ kcal/mol}$			
UC		A	
HIV-1 NEF site:	5' -	CACUG	CCUUUGGAUGGUGCUA -3'
			::
G031-29:	3' -	GUGAC	-GGAAGUUUACACGAU -5'
		UU	
$\Delta G = -35.7 \text{ kcal/mol}$			
UC			
HIV-1 NEF site:	5' -	CACUGACCUUUGGAUGGUGCUA	-3'
			::
G020-29:	3' -	GUGACUGGAAGUUUACACGAU	-5'
		UU	
$\Delta G = -43.4 \text{ kcal/mol}$			

FIG. 22B

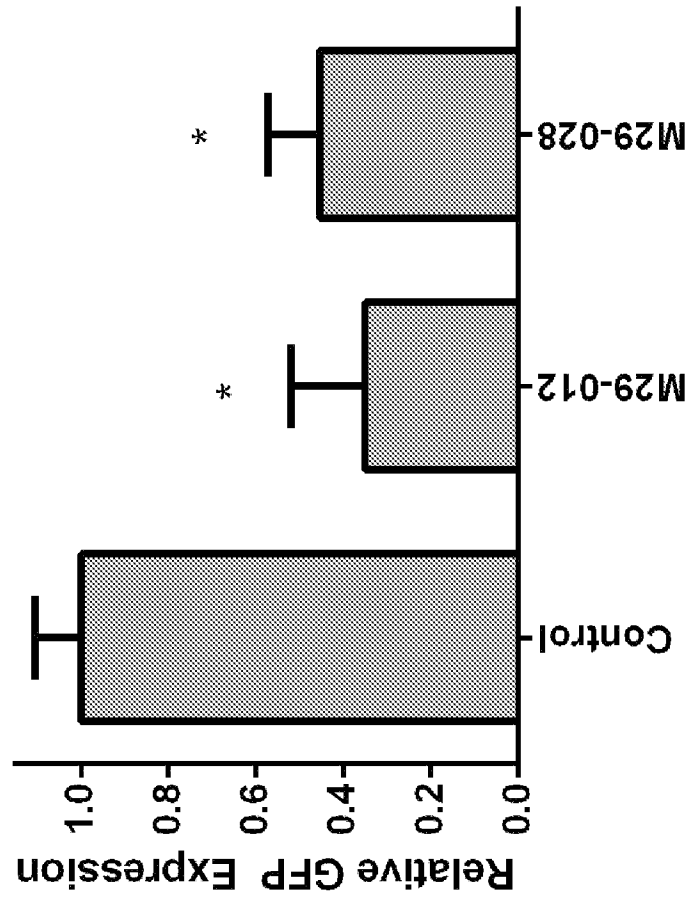


FIG. 22C

FIG. 23A

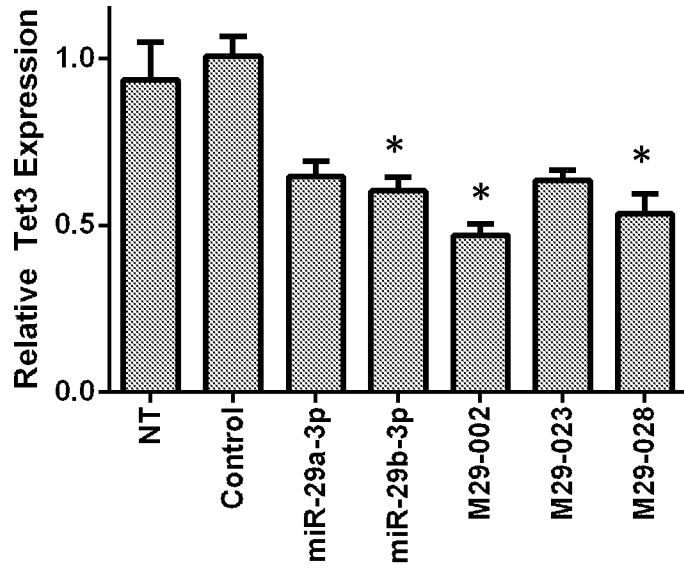


FIG. 23B

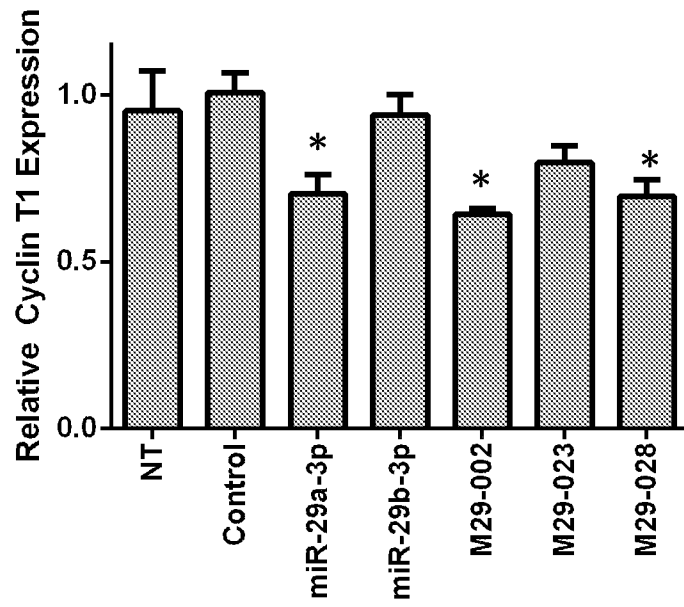
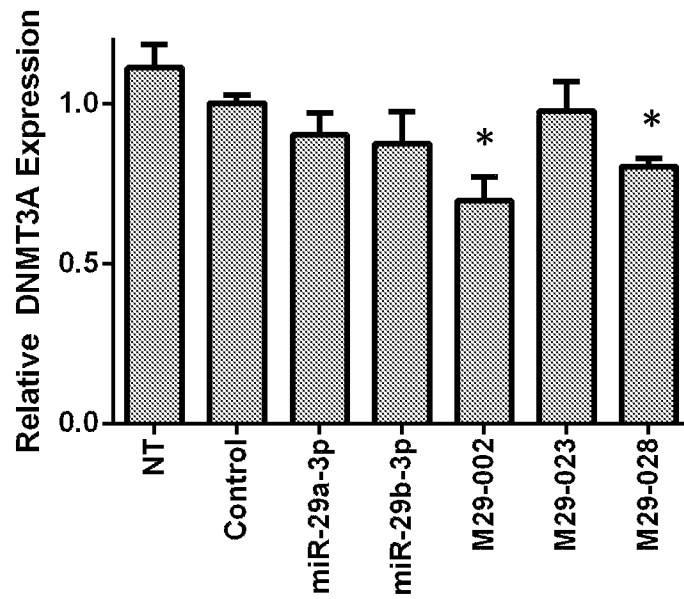


FIG. 23C



Calculated Free Energy Requirements for Target Recognition of Mimic Guide Strands to SARS Viral Transcript

SEQ ID NO:	Guide Strand	Free energy (ΔG)* [kcal/mol]				
		24077	19385	6114	Net	Avg.
12	miR-29a-3p	-21.2	-28.7	-21.8	-71.7	-23.9
13	miR-29b-3p	-23.1	-27.2	-22.2	-72.5	-24.2
102	G003-29	-22.9	-29.7	-21.8	-74.4	-24.8
103	G004-29	-24.9	-27.5	-21.3	-73.7	-24.6
112	G022-29	-28.9	-28.2	-22.4	-79.5	-26.5
115	G025-29	-28.9	-28.8	-22.1	-79.8	-26.6
119	G029-29	-25.1	-28.1	-24.4	-77.6	-25.9
117	G027-29	-25.1	-28.1	-24.1	-77.3	-25.8
105	G006-29	-25.3	-30.0	-20.3	-75.6	-25.2
110	G020-29	-25.5	-30.6	-23.1	-79.2	-26.4
109	G019-29	-29.3	-31.4	-21.1	-81.8	-27.3
100	G001-29	-29.3	-30.7	-21.4	-81.4	-27.1

*Free energy (ΔG) with cognate target sites at nucleotide positions 24077 (SEQ ID NO:476), 19385 (SEQ ID NO:481), and 6114 (SEQ ID 495) in the SARS genome were calculated using RNAhybrid 2.2.

FIG. 24A

SEQ ID NO:	Guide Strand	Free energy (ΔG)* [kcal/mol]				
		10840	19401	26687	Net	Avg.
86	G129-30	-18.4	-17.9	-22.0	-58.3	-19.4
88	G132-30	-16.1	-19.1	-23.5	-58.7	-19.6

*Free energy (ΔG) with cognate target sites at nucleotide positions 10840 (SEQ ID NO: 826), 19401 (SEQ ID NO: 827), and 26687(SEQ ID NO: 828) in the SARS genome were calculated using RNAhybrid 2.2.

FIG. 24B

Calculated Free Energy Requirements for Target Recognition of Mimic Guide Strands to SARS-CoV-2 Viral Transcript

SEQ ID NO:	Guide Strand	Free energy (ΔG)* [kcal/mol]				
		28648	19455	11350	Net	Avg.
12	miR-29a-3p	-23.6	-27.5	-25.6	-76.7	-25.6
13	miR-29b-3p	-24.4	-26.4	-26.0	-76.8	-25.6
102	G003-29	-23.7	-28.9	-27.8	-80.4	-26.8
103	G004-29	-29.4	-27.5	-26.6	-83.5	-27.8
112	G022-29	-23.7	-29.0	-27.3	-80.0	-26.7
115	G025-29	-27.8	-28.9	-27.4	-84.1	-28.0
119	G029-29	-27.0	-26.8	-26.8	-80.6	-26.9
117	G027-29	-29.0	-27.8	-28.4	-85.2	-28.4
105	G006-29	-28.7	-30.0	-28.4	-87.1	-29.0
110	G020-29	-28.3	-30.3	-28.6	-87.2	-29.1
109	G019-29	-27.1	-32.2	-30.2	-89.5	-29.8
100	G001-29	-23.3	-31.5	-29.1	-83.9	-28.0

*Free energy (ΔG) with cognate target sites at nucleotide positions 28648 (SEQ ID NO:500), 19455 (SEQ ID NO:513), and 11350 (SEQ ID NO:518) in the SARS-CoV-2 genome were calculated using RNAhybrid 2.2.

FIG. 25A

SEQ ID NO:	Guide Strand	Free energy (ΔG)* [kcal/mol]				
		10415	20344	26714	Net	Avg.
86	G129-30	-17.7	-20.4	-16.7	-54.8	-18.3
88	G132-30	-17.3	-20.4	-18.9	-56.6	-18.9

*Free energy (ΔG) with cognate target sites at nucleotide positions 10415 (SEQ ID NO: 829), 20344 (SEQ ID NO: 830), and 26714 (SEQ ID NO: 831) in the SARS-CoV2 genome were calculated using RNAhybrid 2.2.

FIG. 25B

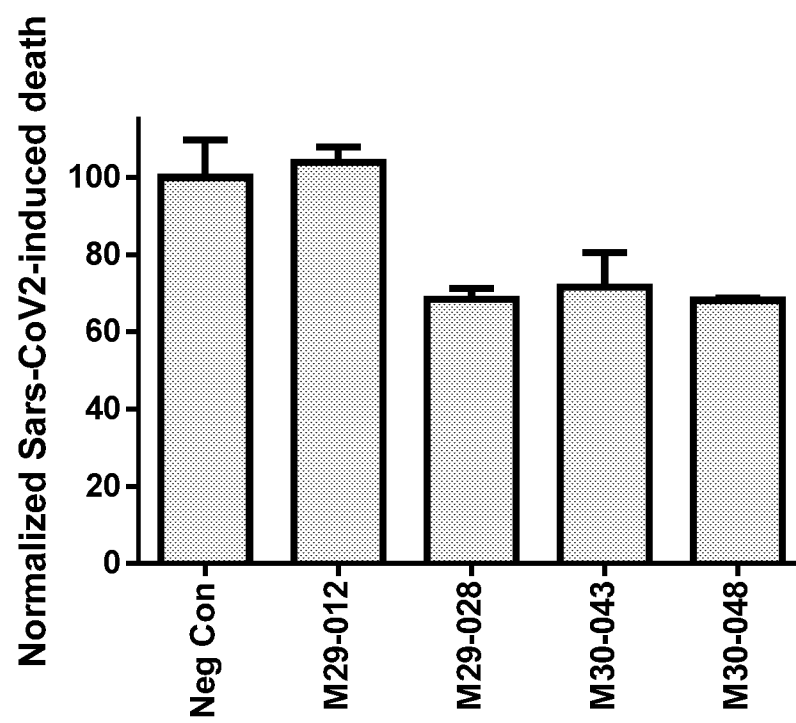


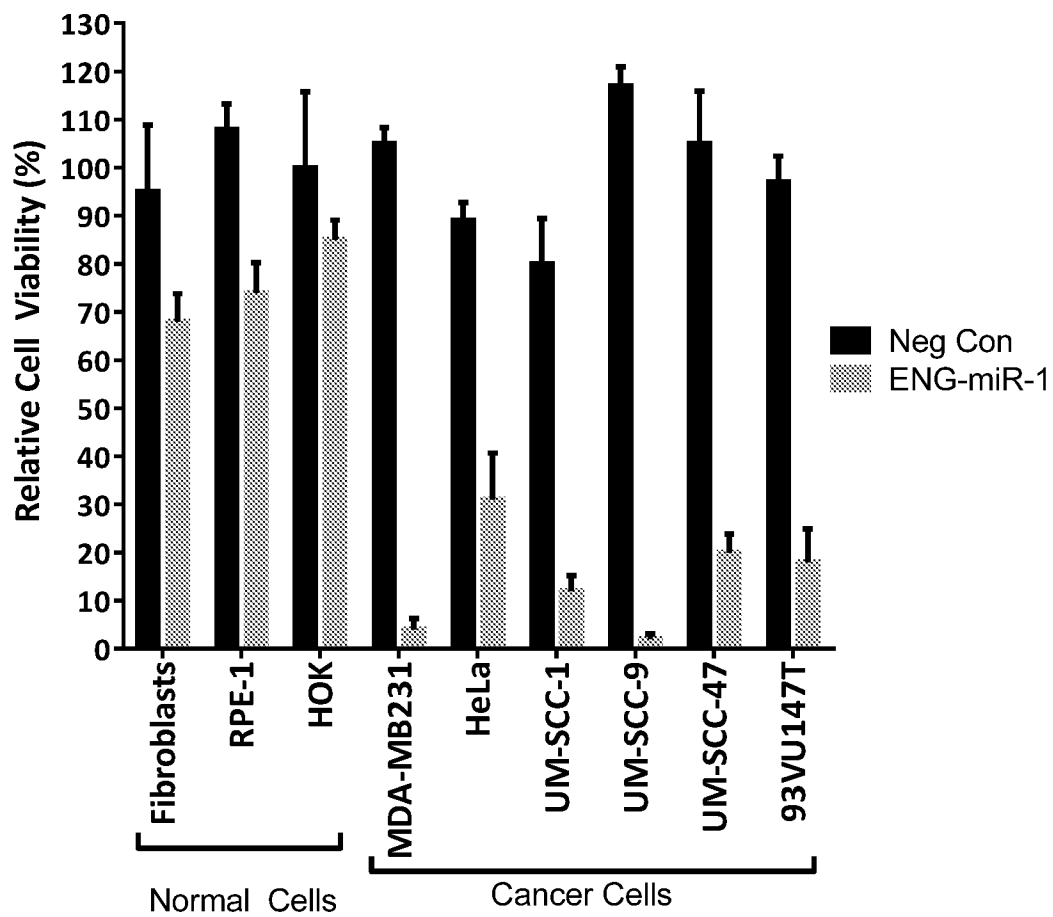
FIG. 25C

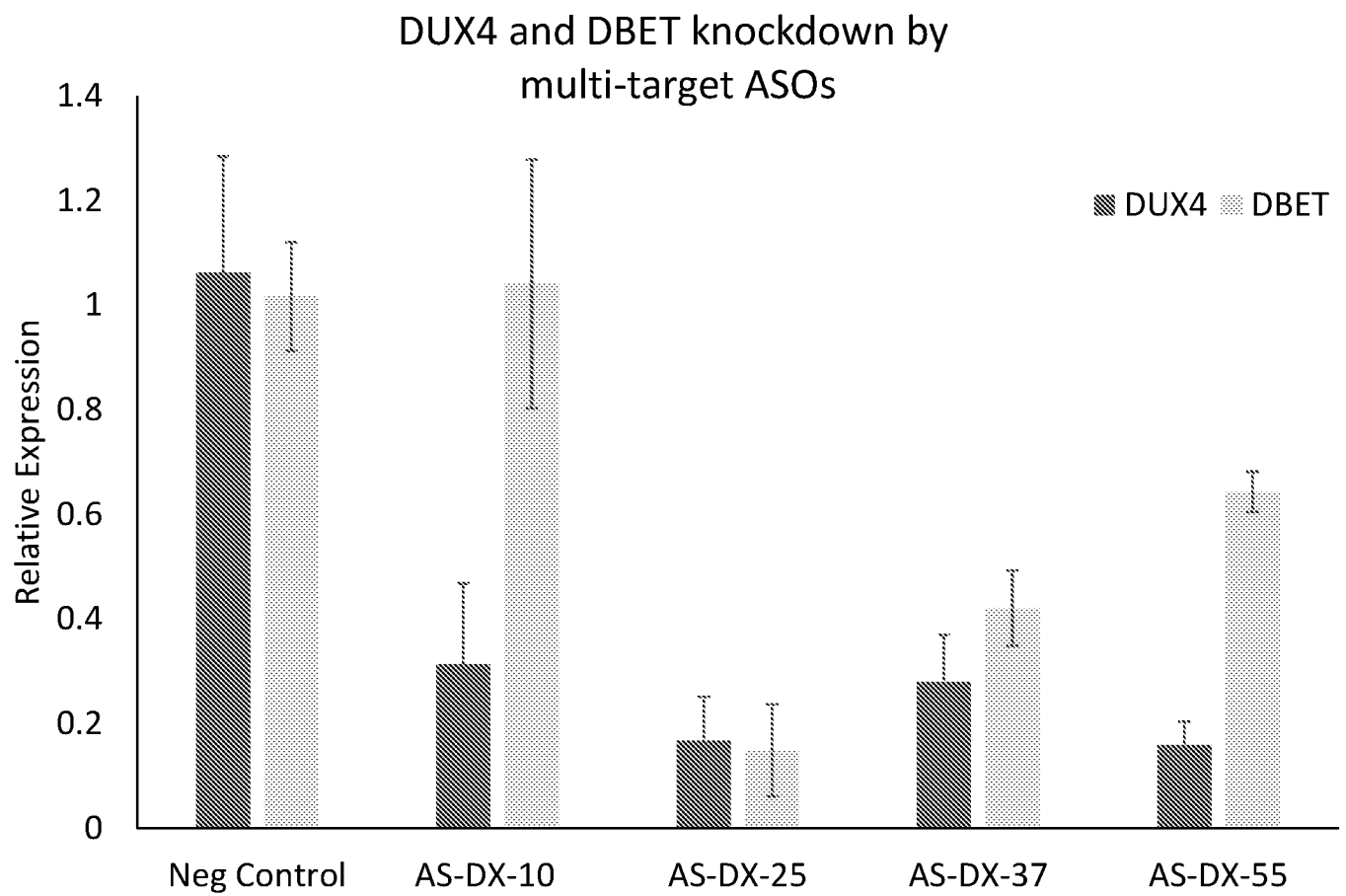
Calculated Free Energy Requirements for Target Recognition of Mimic Guide Strands to HCV Genotype 1 Transcript

SEQ ID NO:	Guide Strand	Free energy (ΔG)* [kcal/mol]				
		3020	2791	240	Net	Avg.
12	miR-29a-3p	-18.7	-18.3	-15.3	-52.3	-17.4
13	miR-29b-3p	-19.0	-21.5	-16.2	-56.7	-18.9
102	G003-29	-18.6	-19.7	-16.0	-54.3	-18.1
103	G004-29	-19.0	-24.7	-17.3	-61.0	-20.3
112	G022-29	-19.0	-24.8	-15.2	-59.0	-19.7
115	G025-29	-19.8	-24.0	-17.5	-61.3	-20.4
119	G029-29	-19.0	-21.7	-17.5	-58.2	-19.4
117	G027-29	-19.0	-23.9	-17.9	-60.8	-20.3
105	G006-29	-18.6	-22.5	-17.1	-58.2	-19.4
110	G020-29	-18.6	-23.5	-17.5	-59.6	-19.9
109	G019-29	-20.0	-21.0	-19.9	-60.9	-20.3
100	G001-29	-18.9	-21.3	-14.9	-55.1	-18.4

*Free energy (ΔG) with cognate target sites at nucleotide positions 3020 (SEQ ID NO:587), 2791 (SEQ ID NO:588), and 240 (SEQ ID NO:589) in HCV Genotype 1 genome were calculated using RNAhybrid 2.2.

FIG. 26

**FIG. 27**

**FIG. 28**

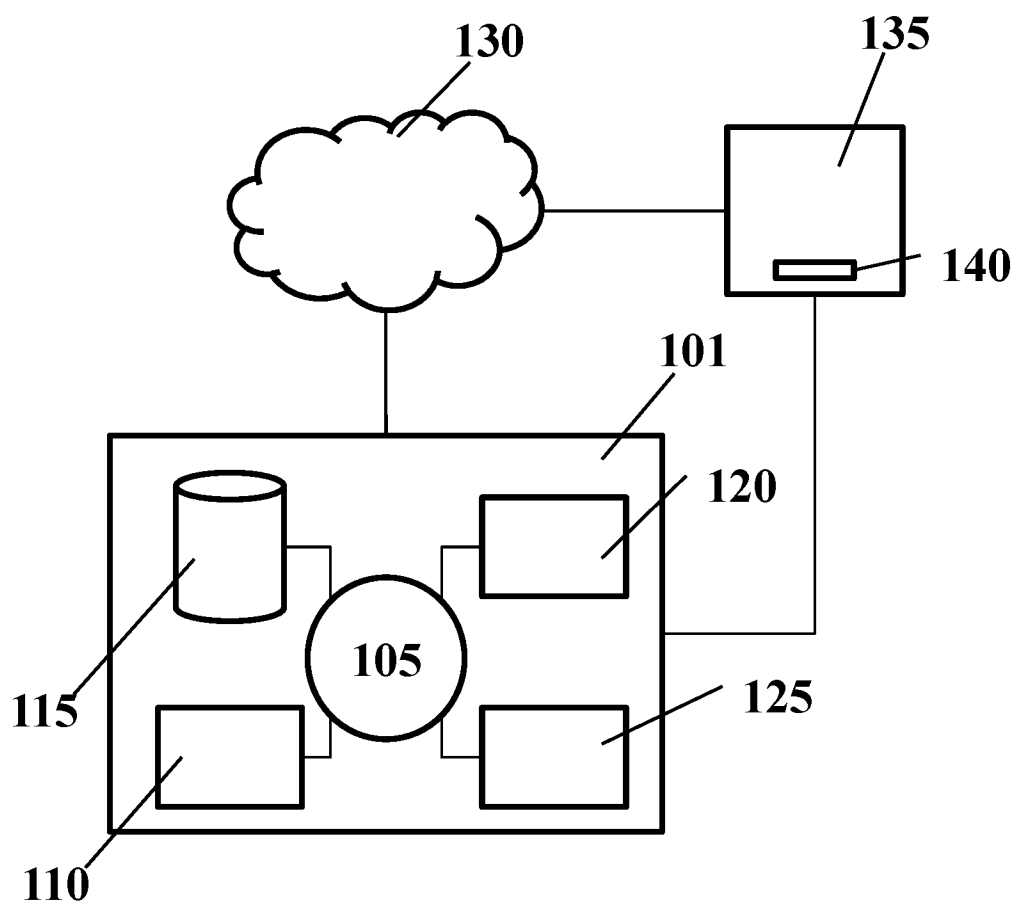
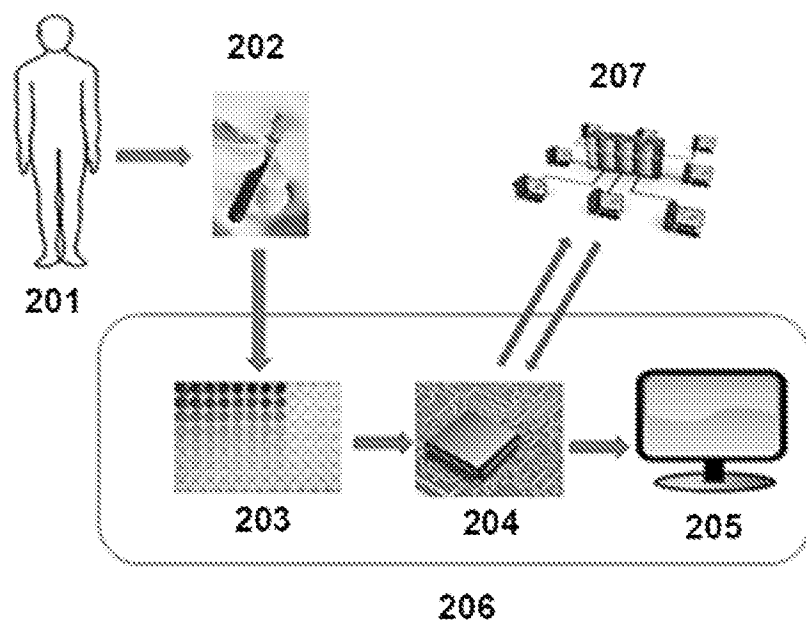


FIG. 29

**FIG. 30**