

<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	UGUAAACAUCCUGCGACUGGAAG
SEQ ID NO: 38	G006-30	UGUAAACAUCCUGCGACUGGAA-
SEQ ID NO: 40	G061-30	UGUAAACAUCCCGCGACUGGAAG
SEQ ID NO: 41	G062-30	UGUAAACAUCCUGUGACUGGAAG
SEQ ID NO: 42	G063-30	UGUAAACAUCCCGUGACUGGAAG
SEQ ID NO: 43	G064-30	UGUAAACAUCCUGACACUCUCAGC
SEQ ID NO: 44	G065-30	UGUAAACAUCCUGACACUCUCAG-
SEQ ID NO: 45	G066-30	UGUAAACAUCCUGACACUCUCA--

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

SEQ ID NO: 467 **ITGA6 3'UTR:** 5' - A U ACAAAUAUAUUU A
 UUC UAGUC UGUUUACA -3'
 ||| :||| |||||
 SEQ ID NO: 1 **miR-30a-5p:** 3' - AAG-GUCAG ACAAUGU- -5'
 G CUCCU-----

$$\Delta G = -17.4 \text{ kcal/mol}$$

SEQ ID NO: 468 **SERPINE1 3'UTR:** 5' - A UU AG U UGACU U
 UU GG UG AGG UGUUUAC -3'
 || :| || ||| |||||
 SEQ ID NO: 1 **miR-30a-5p:** 3' - AA UC GC-UCC ACAAUG -5'
 G GG A- U---- U

$$\Delta G = -17.5 \text{ kcal/mol}$$

SEQ ID NO: 469 **EGFR 3'UTR:** 5' - AGA UU CAAC C
 CUGGUU G GUUUACA -3'
 |::||: | |||||
 SEQ ID NO: 1 **miR-30a-5p:** 3' - GGUCAG C CAAUGU- -5'
 GAA CU CUA

$$\Delta G = -15.5 \text{ kcal/mol}$$

FIG. 2A

SEQ ID NO: 467 **ITGA6 3'UTR:** 5' - A U A AAAUAUAUUU A
 UUC UAGUC CA UGUUUACA -3'
 ||| :||| || |||||
 SEQ ID NO: 39 **G007-30:** 3' - AAG-GUCAG GU ACAAUGU- -5'
 G C CCU-----

$$\Delta G = -19.0 \text{ kcal/mol}$$

SEQ ID NO: 468 **SERPINE1 3'UTR:** 5' - A UU AG UGACU U
 UU GG UGUAGG UGUUUAC -3'
 || :| ||:||| |||||
 SEQ ID NO: 39 **G007-30:** 3' - AA UC GCGUCC ACAAUG -5'
 G GG A- U---- U

$$\Delta G = -22.4 \text{ kcal/mol}$$

SEQ ID NO: 469 **EGFR 3'UTR:** 5' - AGA UU AC-- C
 CUGGU UGCA GUUUACA -3'
 |::|| :||| |||||
 SEQ ID NO: 39 **G007-30:** 3' - GGUCA--GCGU CAAUGU- -5'
 GAA CCUA

$$\Delta G = -18.6 \text{ kcal/mol}$$

FIG. 2B

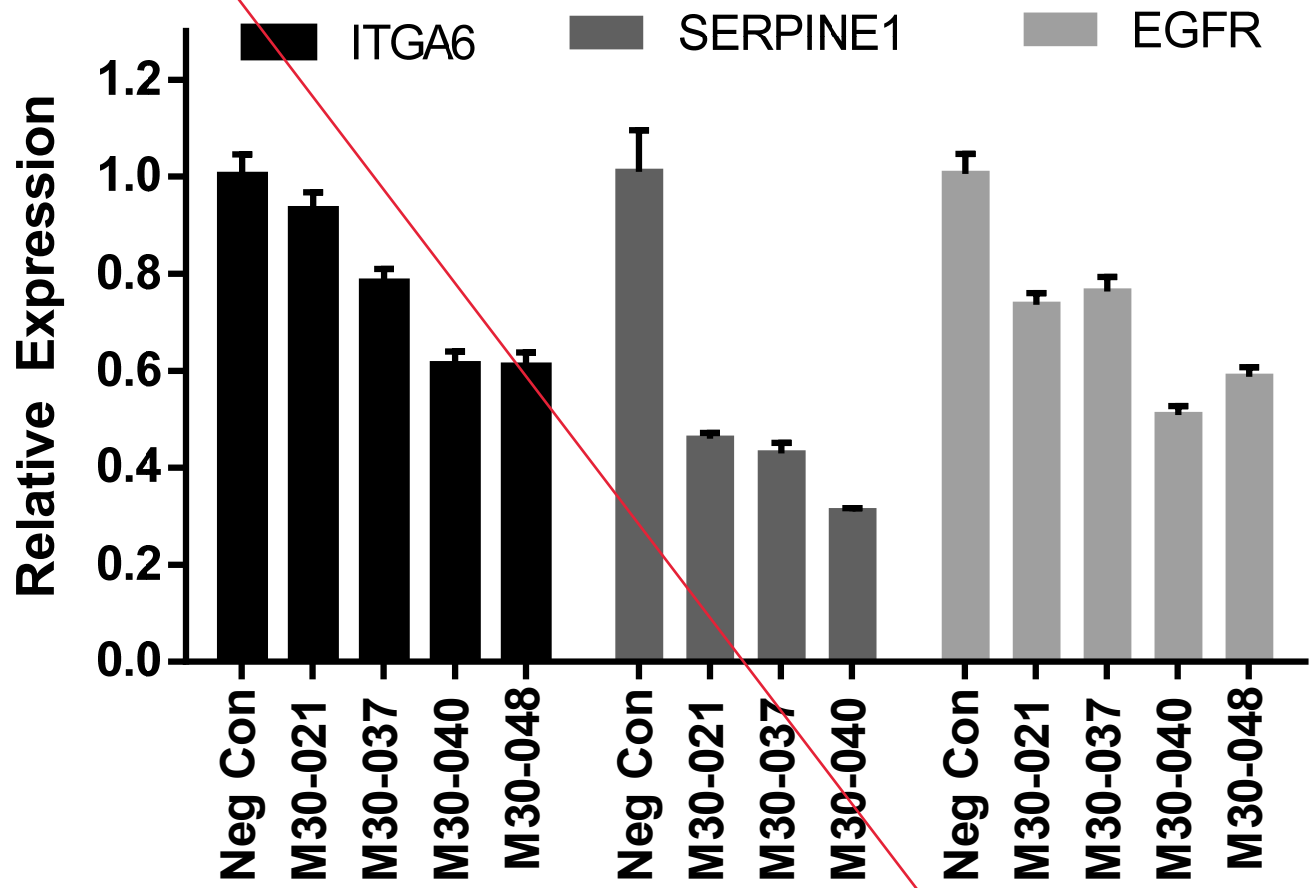
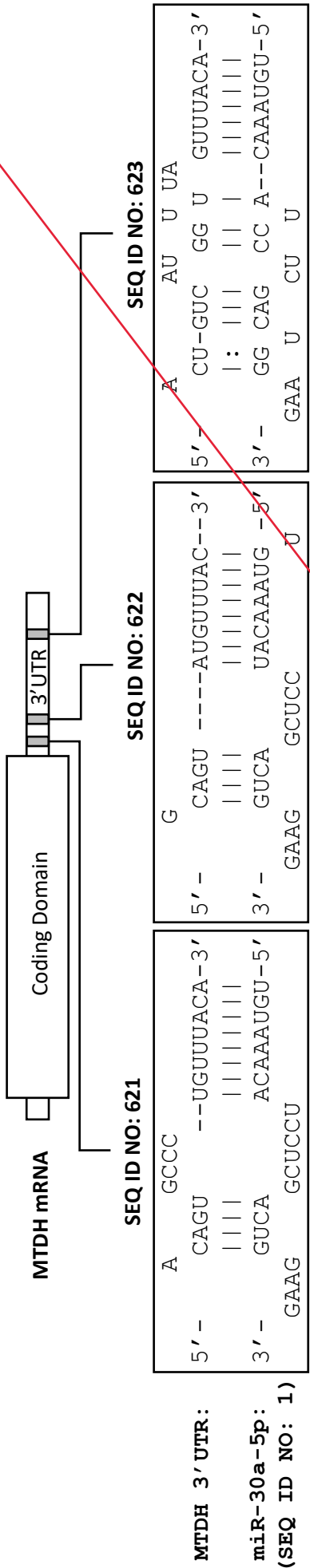


FIG. 2C



MTDH 3'UTR:

miR-30a-5p:

(SEQ ID NO: 1)

SEQ ID NO:	Strand	SEQ ID NO:			NET	Avg
1	miR-30a-5p	621	622	623	-46.5	-15.5
2	miR-30b-5p	-14.9	-13.9	-15.2	-44.0	-14.7
3	miR-30c-5p	-14.9	-14	-14.4	-43.3	-14.4
4	miR-30d-5p	-15.4	-14.6	-17	-47.0	-15.7
5	miR-30e-5p	-15.4	-14.6	-19.6	-49.6	-16.5
39	G007-30	-18.3	-19.4	-17.1	-54.8	-18.3
624	G075-30	-15.5	-16.3	-19.5	-51.3	-17.1
40	G061-30	-18.3	-15.6	-18.2	-52.1	-17.4
41	G062-30	-16.3	-17.9	-19.9	-54.1	-18.0
625	G076-30	-13.8	-17.1	-26.7	-57.6	-19.2
626	G077-30	-15.4	-19	-17.2	-51.6	-17.2
627	G078-30	-18.3	-19.5	-17.9	-55.7	-18.6

Hybridization Free Energy (kcal/mol)

FIG. 3

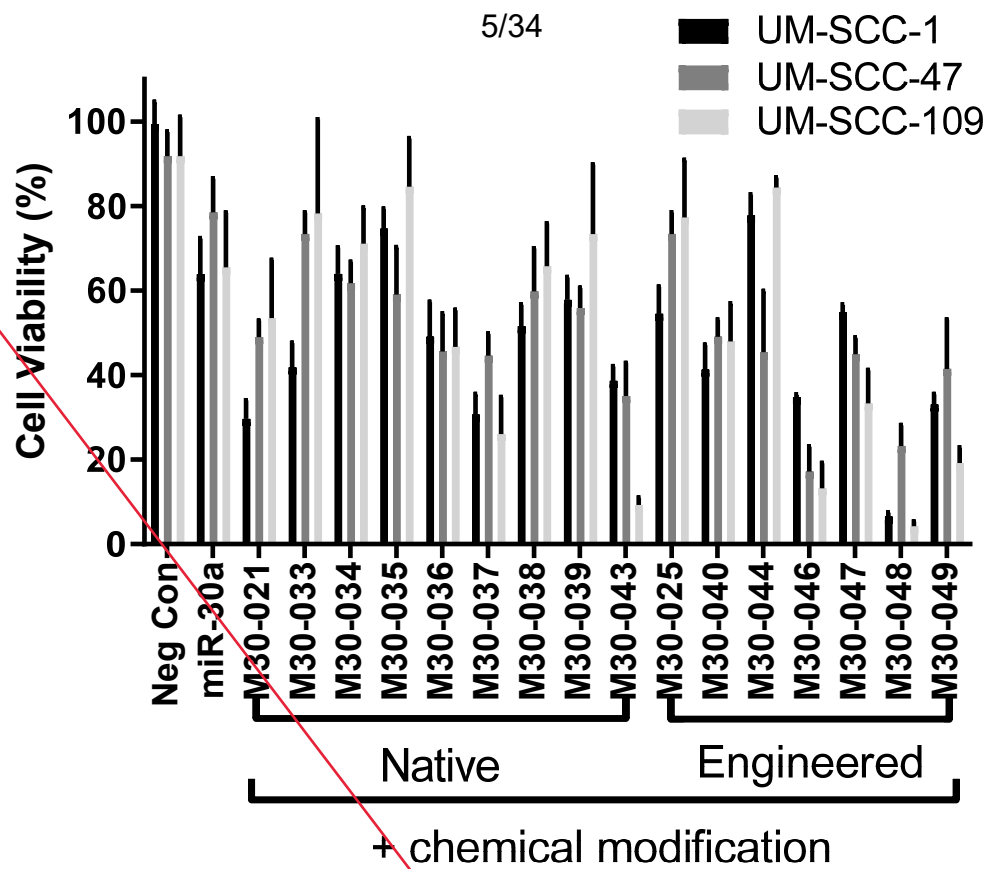


FIG. 4A

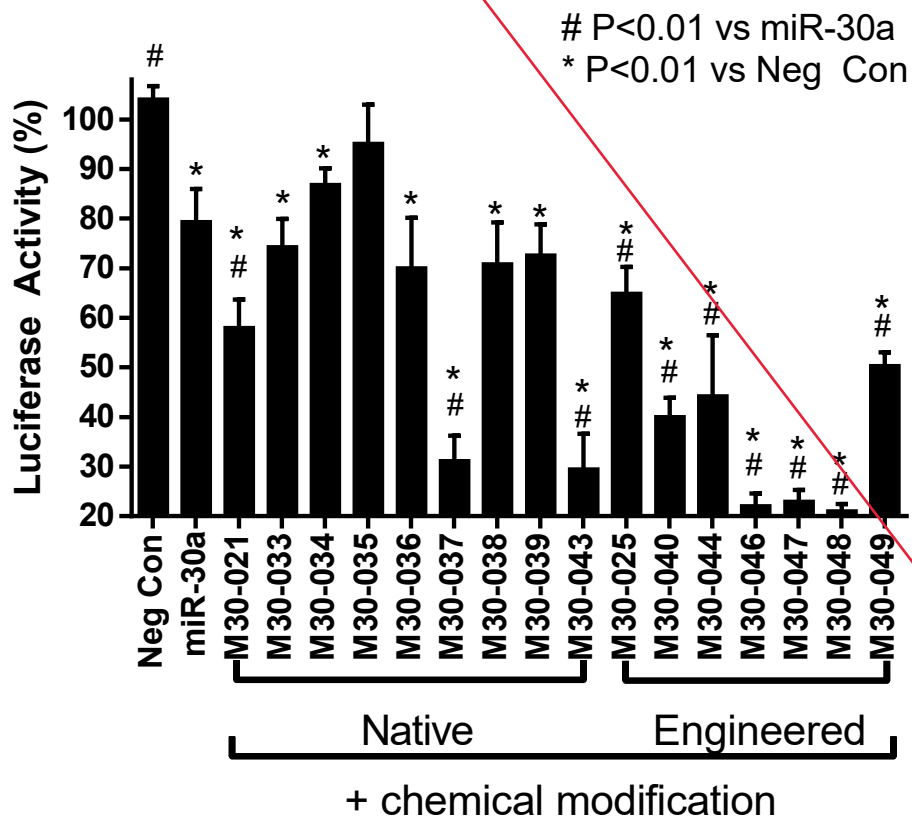


FIG. 4B

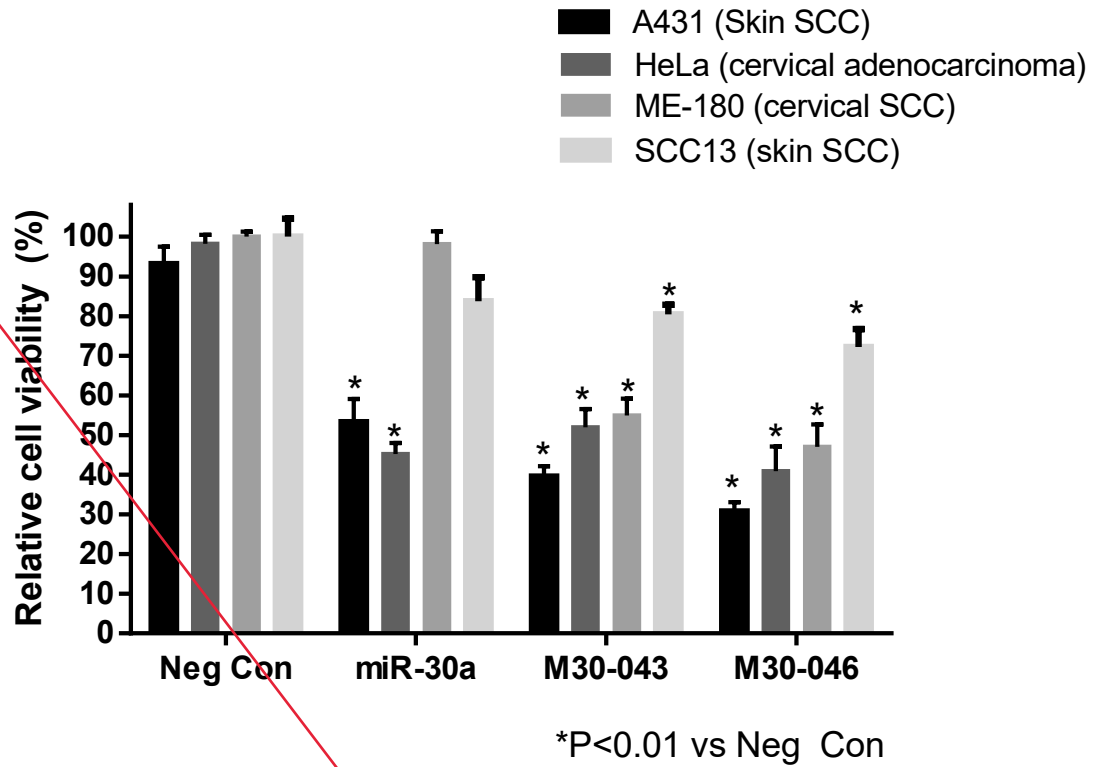


FIG. 4C

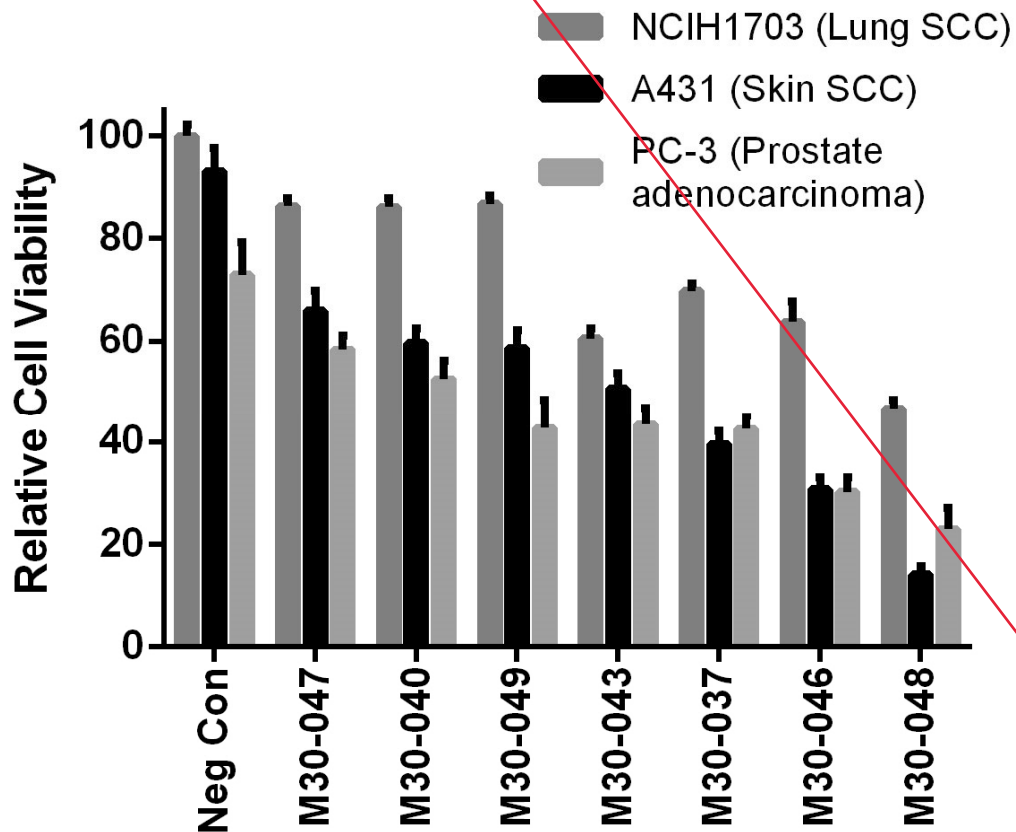


FIG. 4D

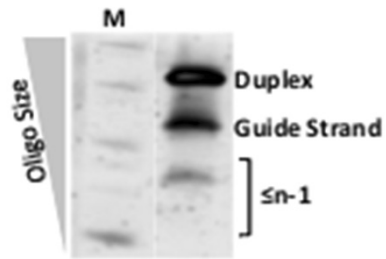


FIG. 5A

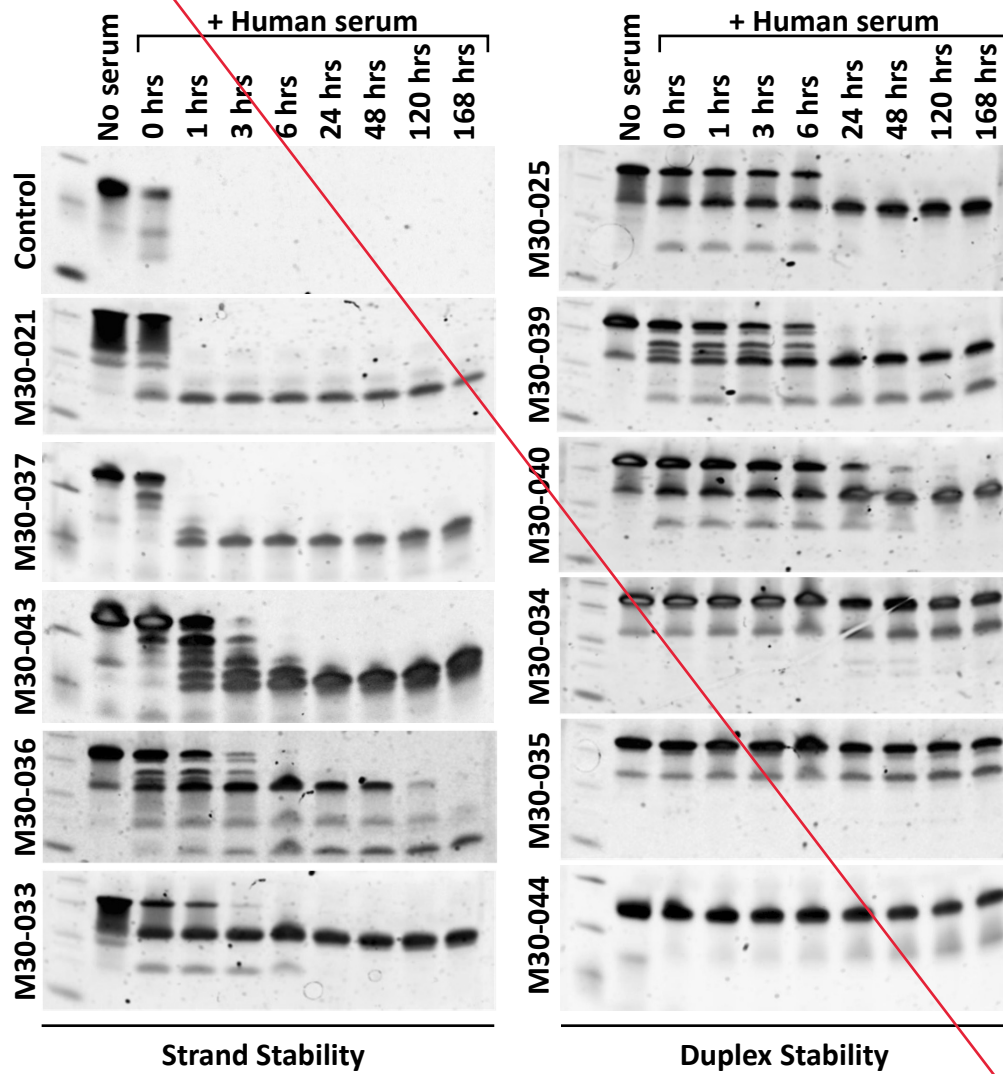


FIG. 5B



FIG. 6A

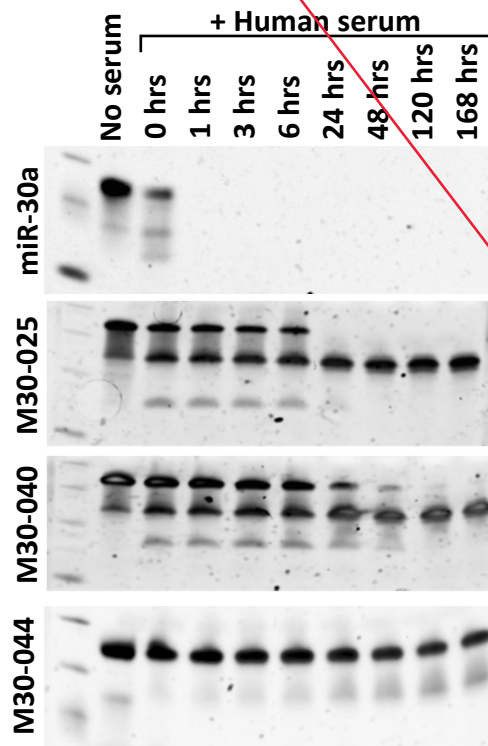
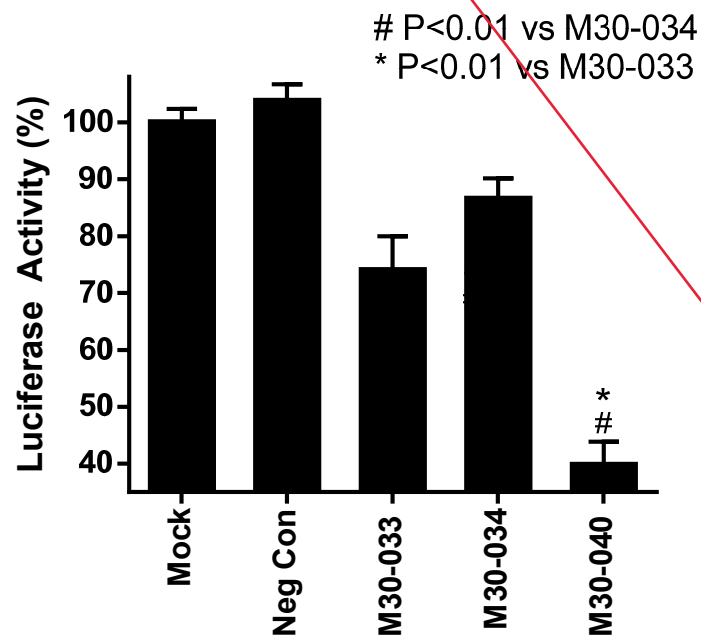
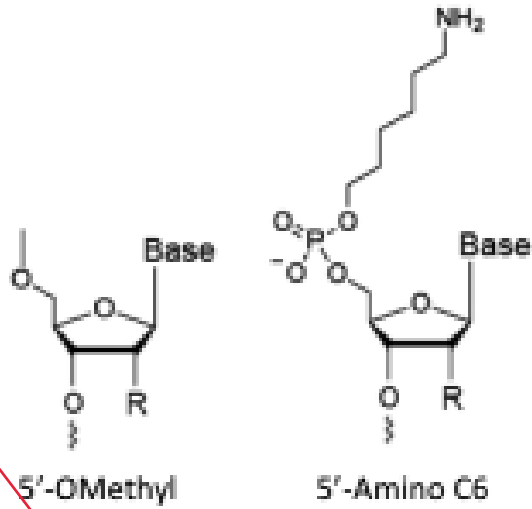
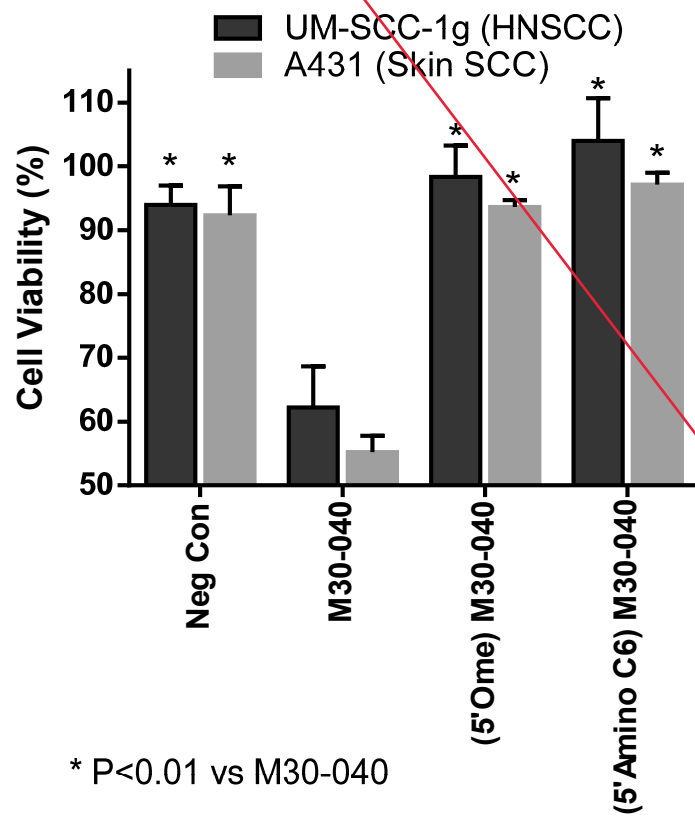


FIG. 6B

FIG. 7B



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

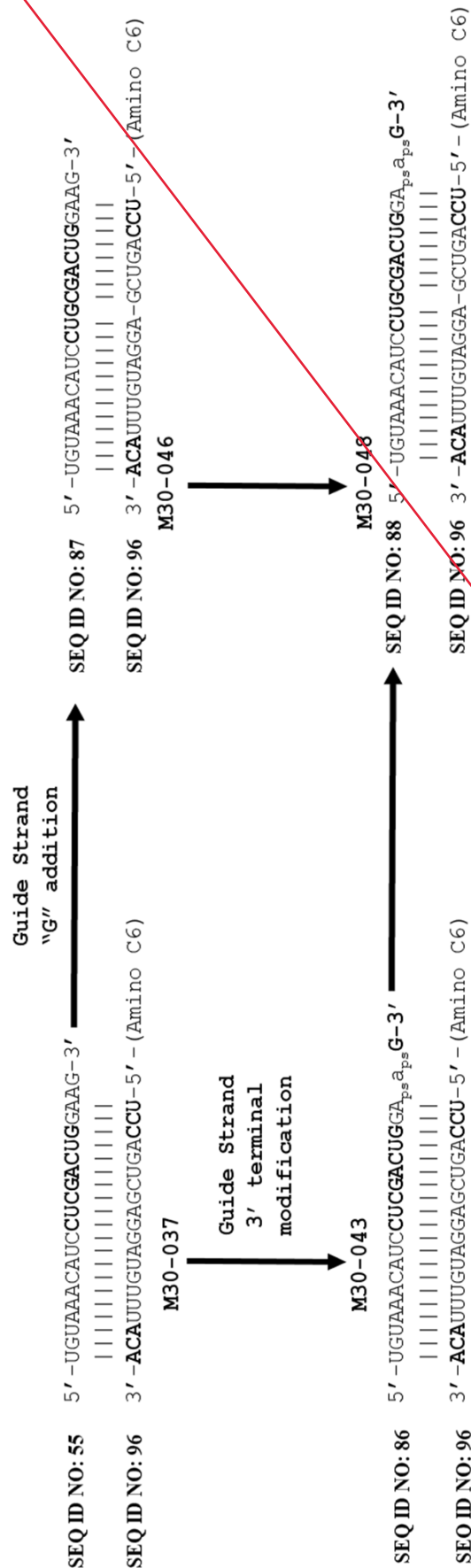


FIG. 9A

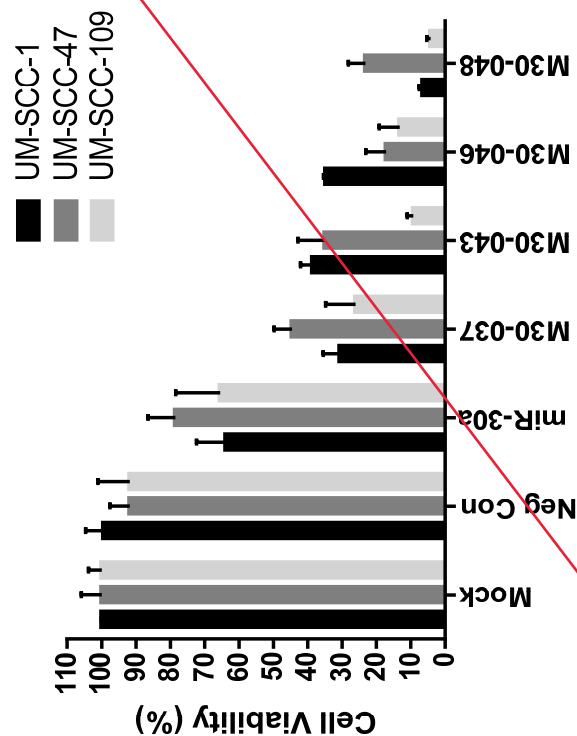


FIG. 9B

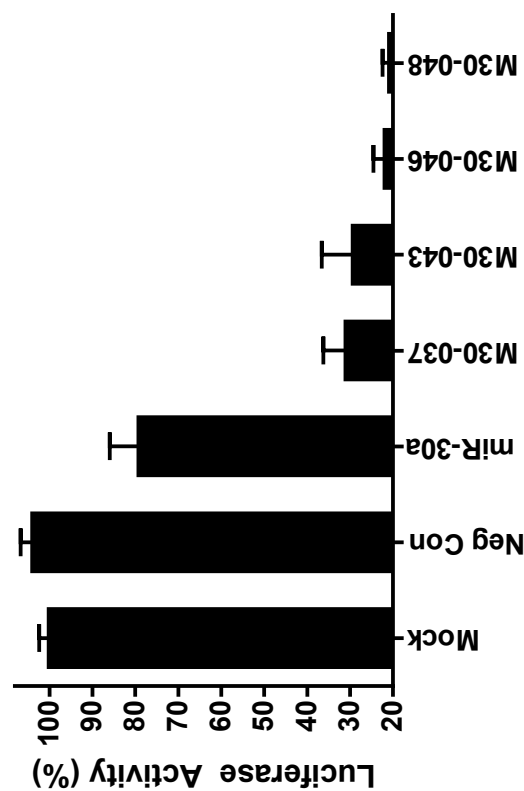


FIG. 9C

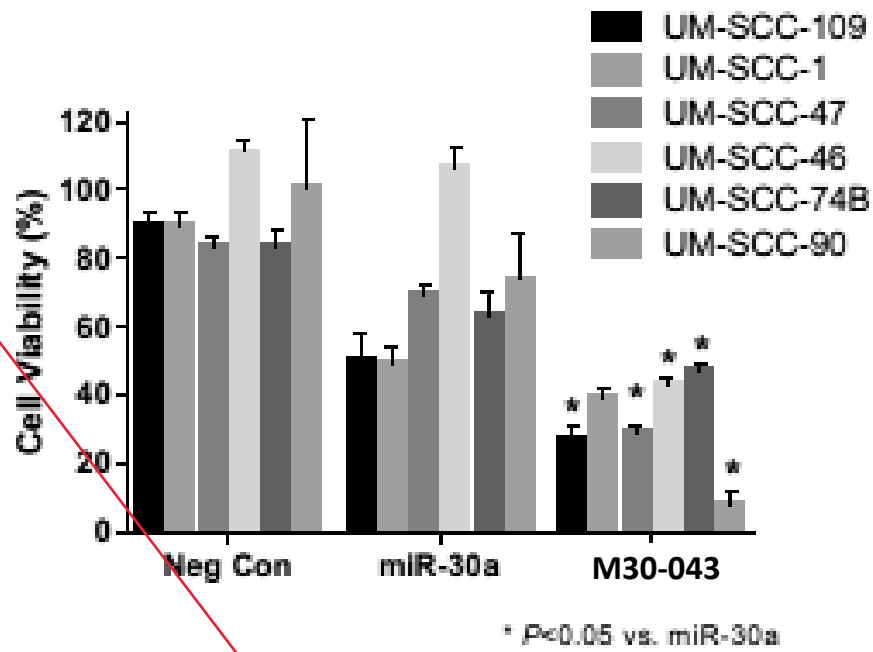


FIG. 10A

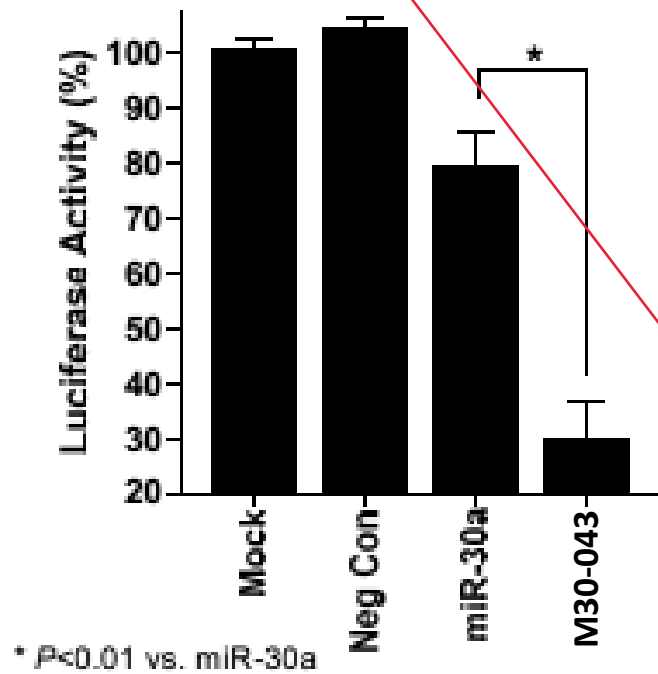


FIG. 10B

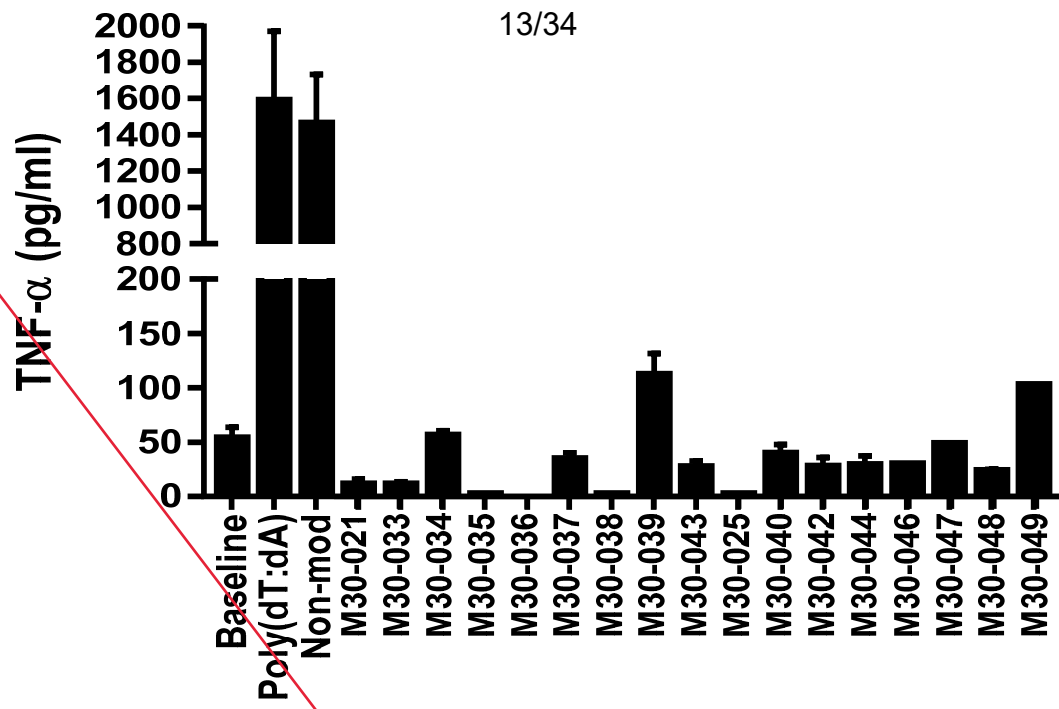


FIG. 11A

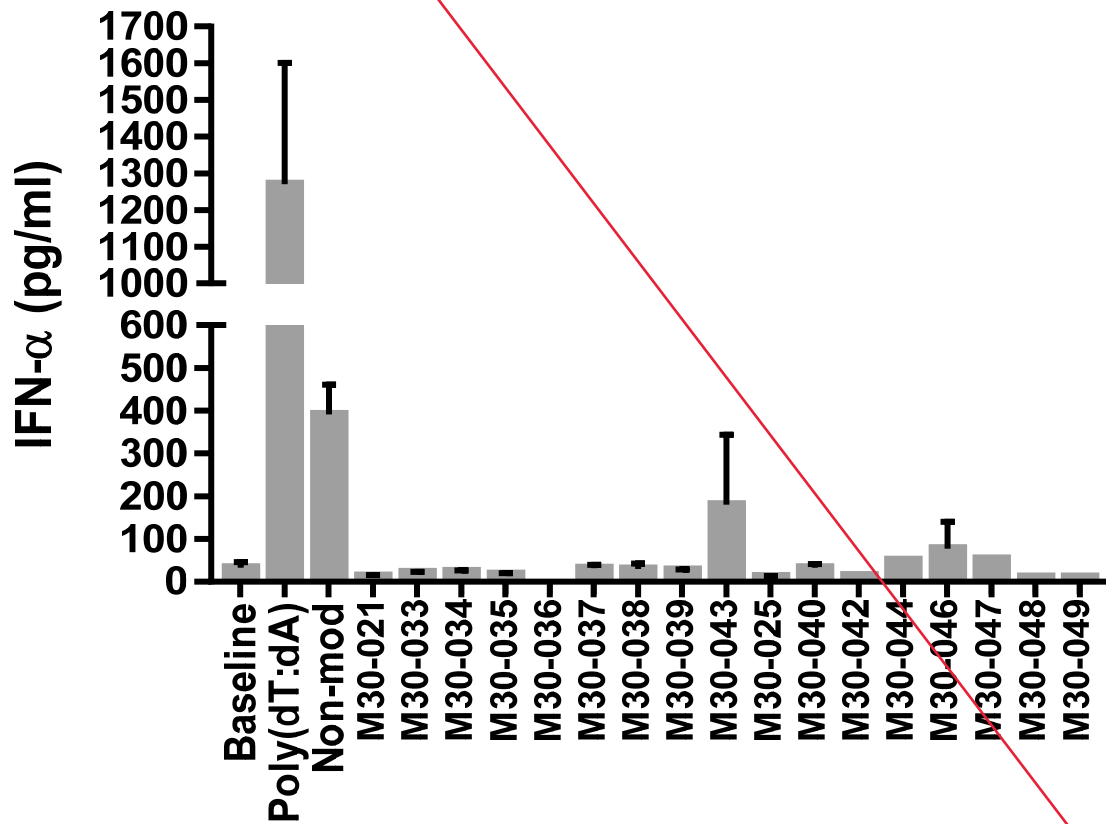


FIG. 11B

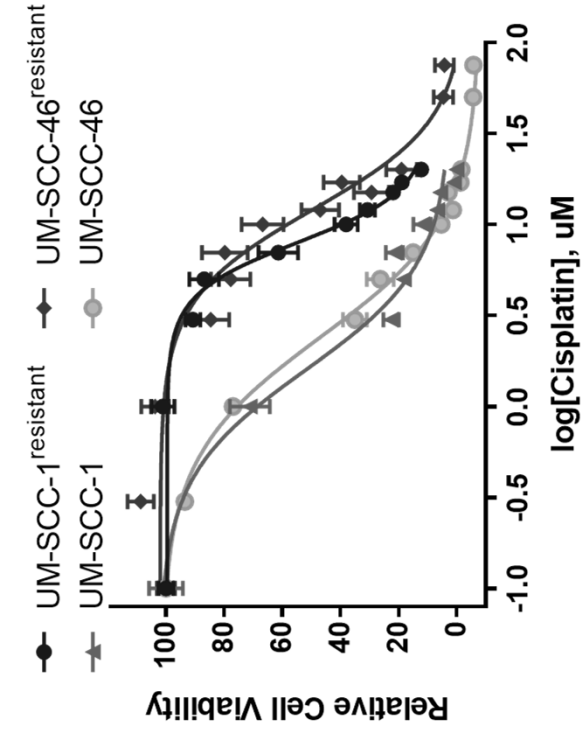


FIG. 12A

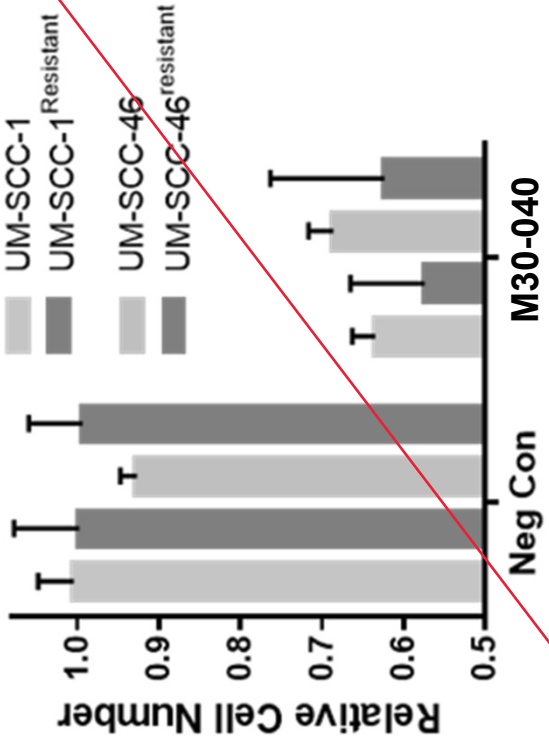


FIG. 12B

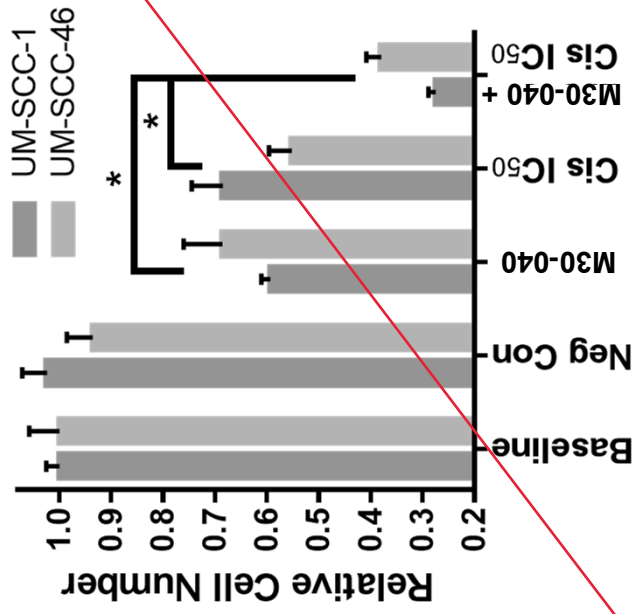


FIG. 12C

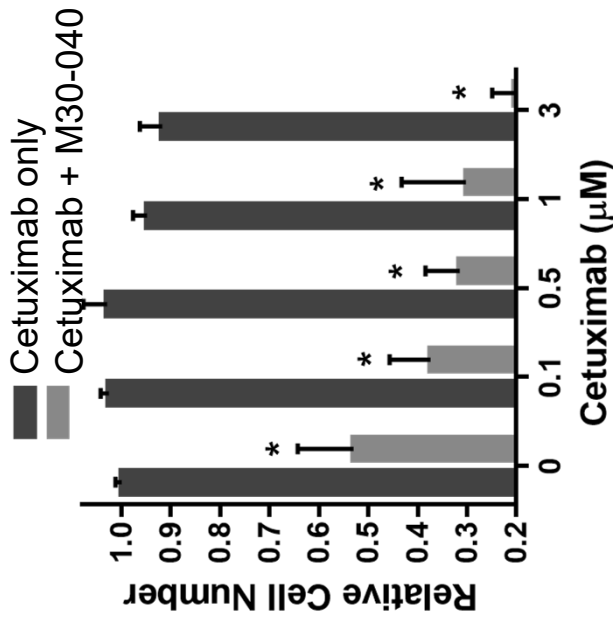
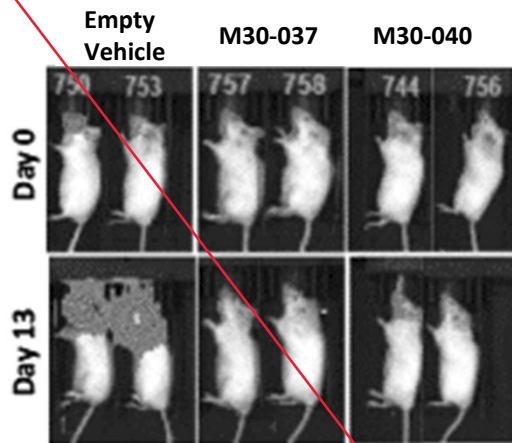
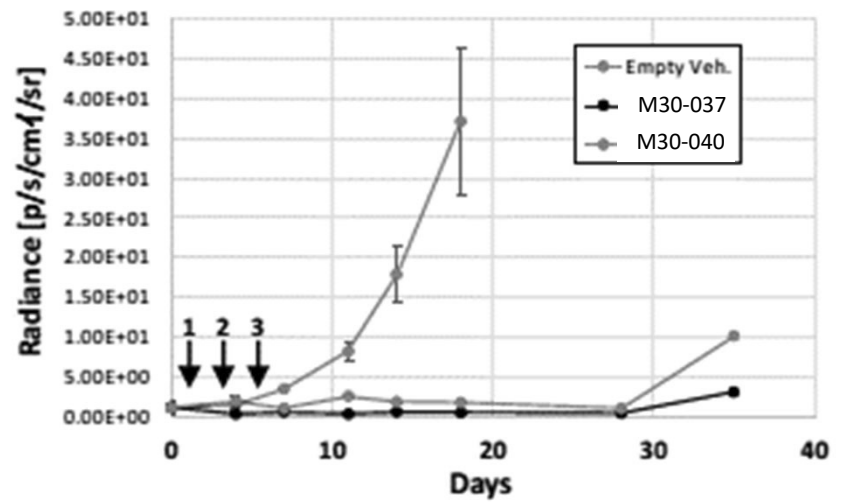
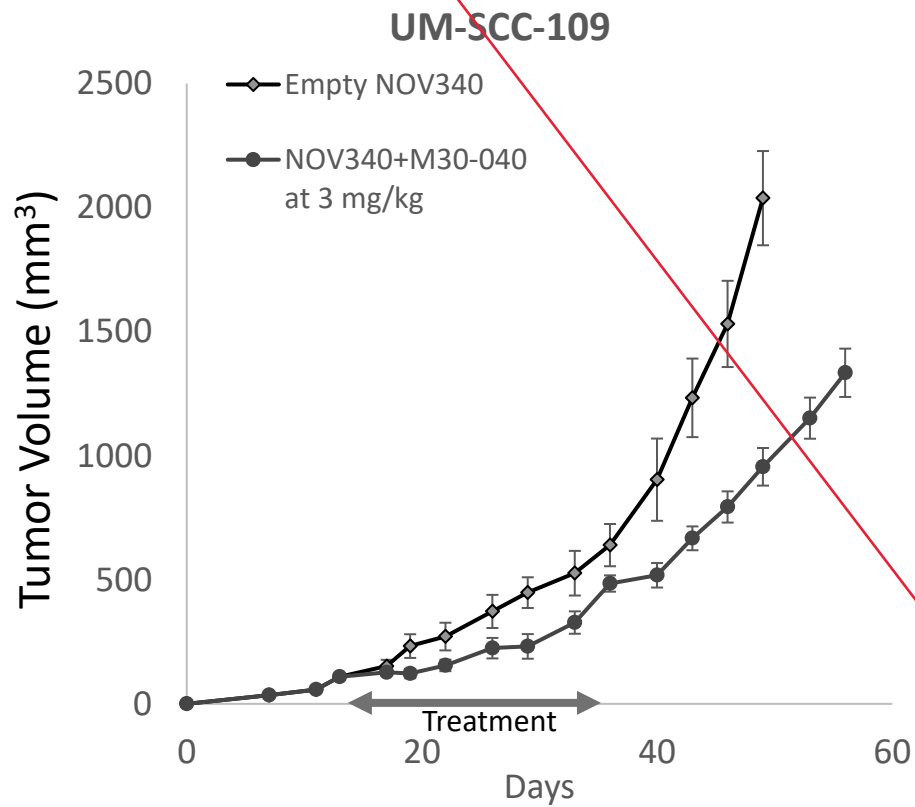
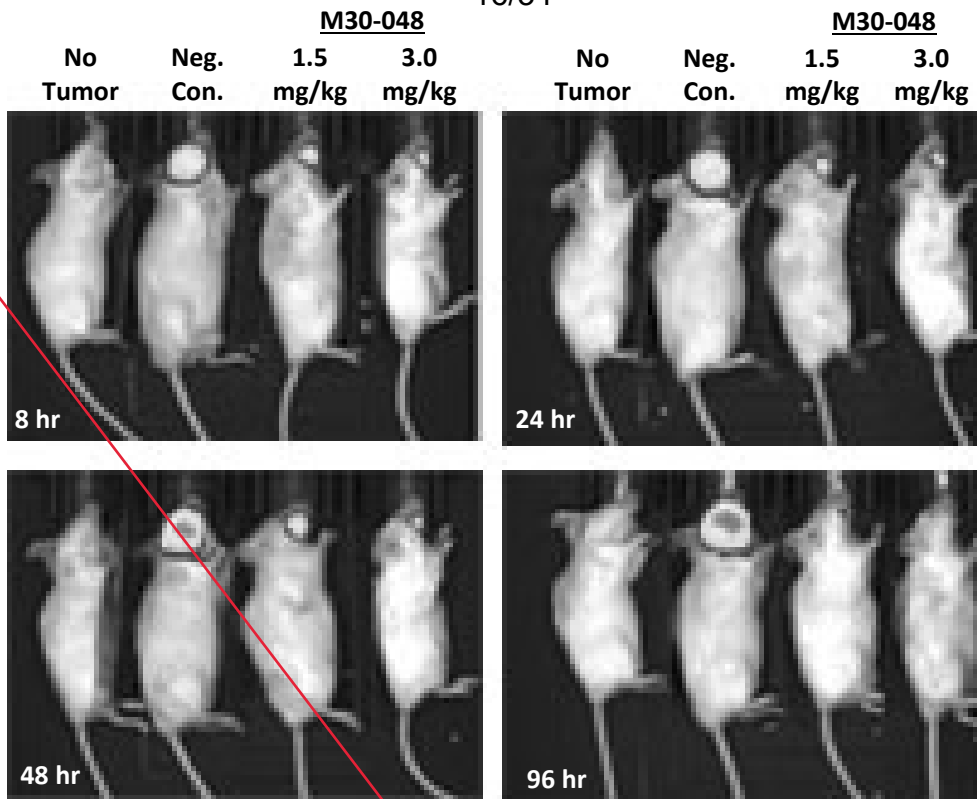
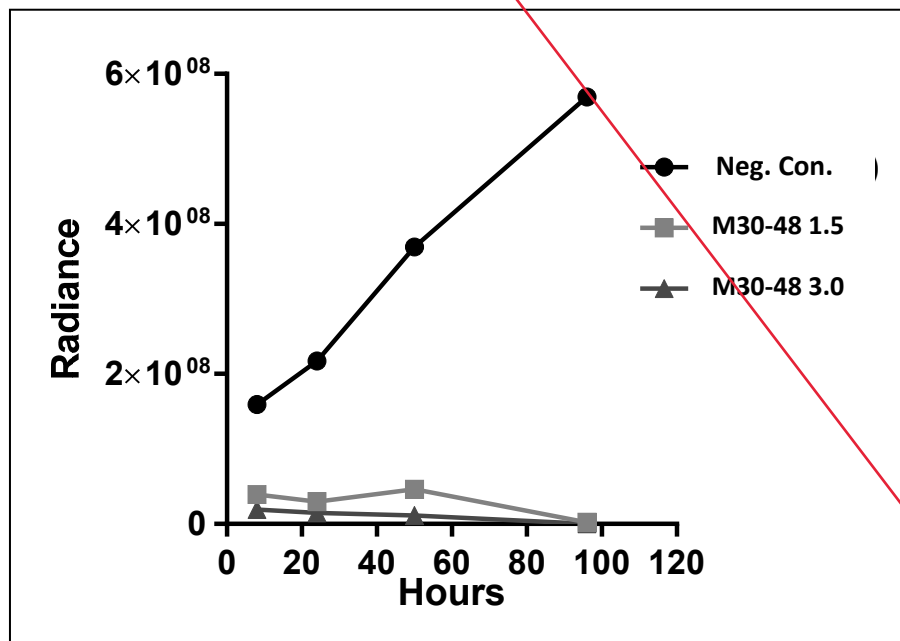


FIG. 12D



**FIG. 14A****FIG. 14B**

		<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 12	Natural	miR-29a-3p	UAGCACCAUCUGAAAUCGGUUA	
SEQ ID NO: 13		miR-29b-3p	UAGCACCAUUUGAAAUCAGUGUU	
SEQ ID NO: 14		miR-29c-3p	UAGCACCAUUUGAAAUCGGUUA	
SEQ ID NO: 102	Engineered	G003-29	UAGCACCAUCUGAAAUCAGUGUU	
SEQ ID NO: 101		G002-29	UAGCACCAUCUGAAAUCAGUGU-	
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	UAGCACCAUCUGAAGUCAGUGUU	
SEQ ID NO: 110		G020-29	UAGCACCAUCUGAAGGUCAGUGUU	
SEQ ID NO: 109		G019-29	UAGCACCAUCUGAAGGCAGUGUU	
SEQ ID NO: 100		G001-29	UAGCACCAUCUGAAAGCAGUGUU	
			Hybrid	
			Mutation	
			Insert.	
			Mut. + Insert.	
			Hybrid + Mut. + insert.	

FIG. 15

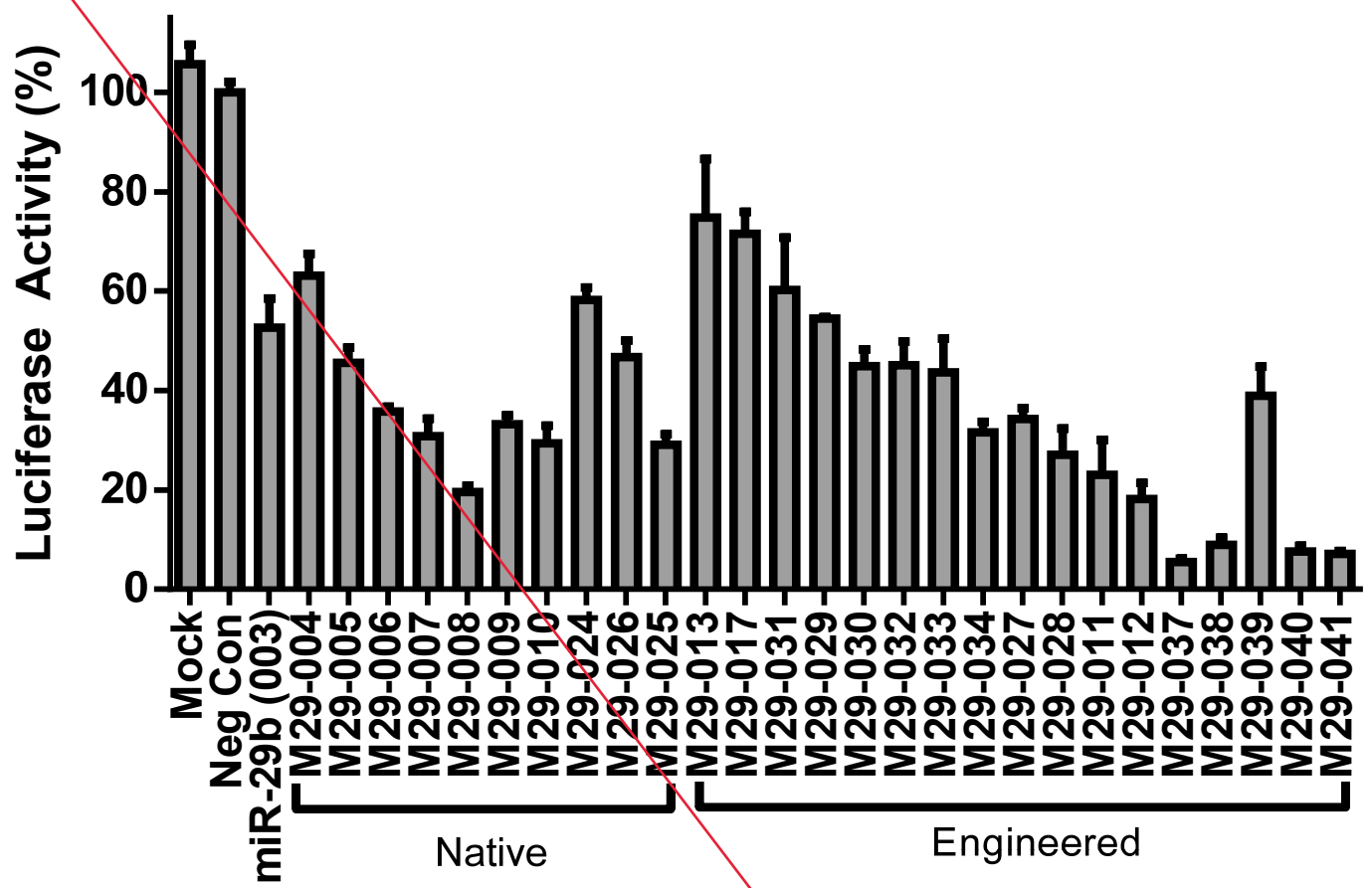


FIG. 17

miR-29b-1:

M29-004:

M29-012:

U GU

(Amino C6)-5'-GCUGGUUUCA AUGGUG UUA-3'

:|||:||||| ||||| :||

3'-UUGUGACUAAAGU UACCAC GAU-5'

U --

U GU

(Amino C6)-5'-GCUGGUUUCA AUGGUG UUA-3'

:|||:||||| ||||| :||

3'-UUGUGACUAAAGU UACCAC GAU-5'

U --

(Amino C6)-5'-CACUGAUUUCAGAUGGUGUUA-3'

|||||:||||| ||||| :||

3'-UUGUGACUAAAGUCUACCACGAU-5'

SEQ ID NO: 16

SEQ ID NO: 13

SEQ ID NO: 170

SEQ ID NO: 13

SEQ ID NO: 176

SEQ ID NO: 102

FIG. 18A

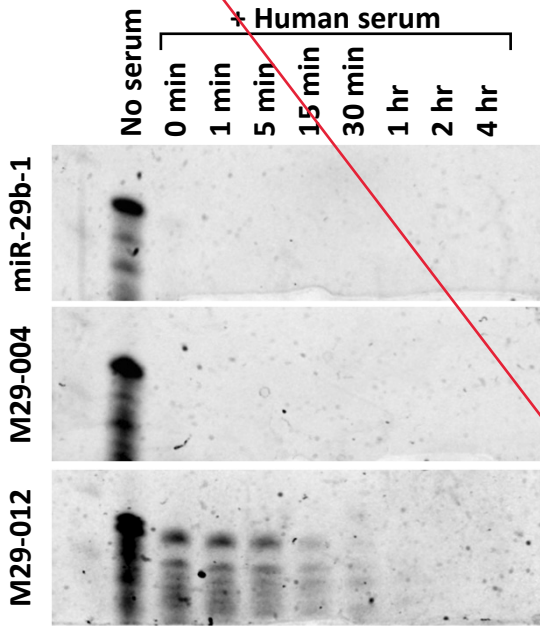


FIG. 18B

M29-024:

(Amino C6)-5'-ACUGAUUUCAGAU^{GU}GUGUUA-3'
 |||||:|||||:
3'-UuGuGaCuAaAgUuUaCcAcGaU-5'

SEQ ID NO:173
SEQ ID NO:127

M29-026:

(Amino C6)-5'-GCUGGUUUCAGAU^{GU}GUGUUA-3'
 :||||:|||||:|:
3'-UuGuGaCuAaAgUuUaCcAc GaU-5'

SEQ ID NO:171
SEQ ID NO:127

M29-028:

(Amino C6)-5'-CACUGAUUUCAGAU^{GU}GUGUUA-3'
 |||||:|||||:
3'-UuGuGaCuAaAgUcUaCcAcGaU-5'

SEQ ID NO:176
SEQ ID NO:128

FIG. 19A

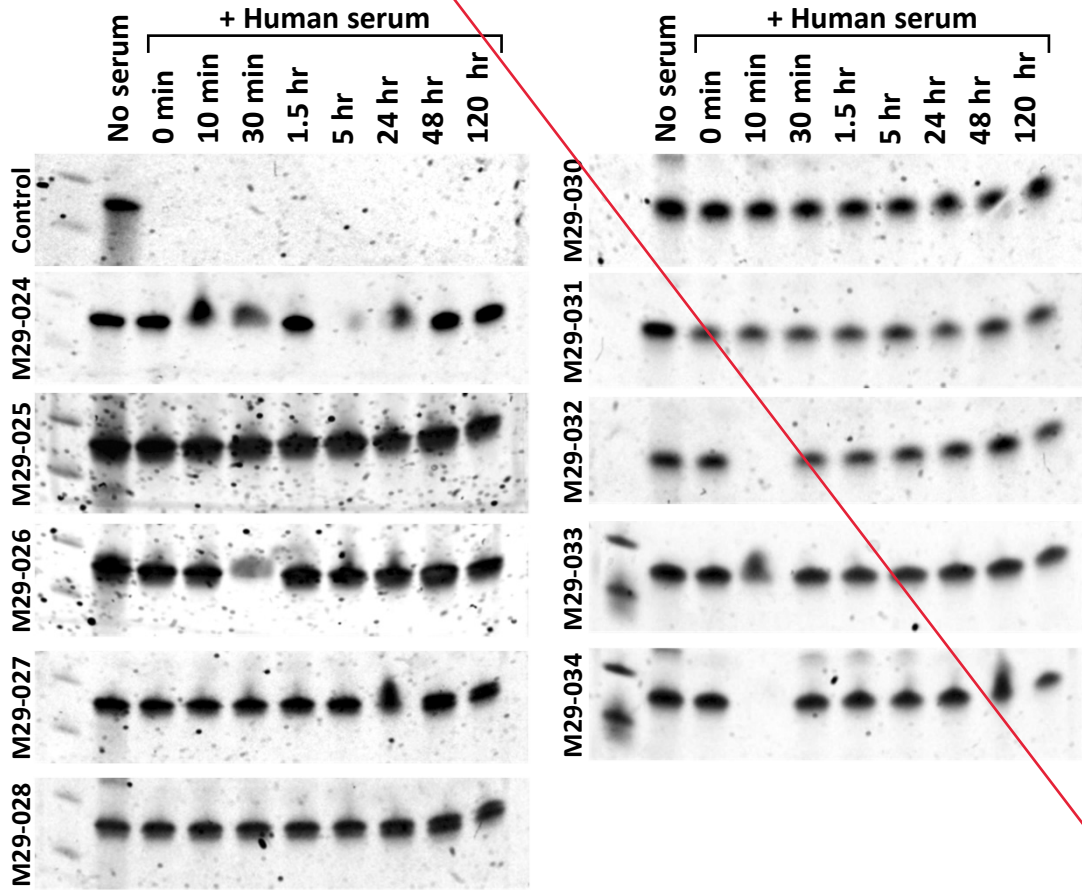


FIG. 19B

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

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

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

FIG. 20A

miR-29b-1
 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' - ACUGAUUUCAGAUUGGUGUUA-3' P007-29 SEQ ID NO: 173
 M29-007 |||||:|||:|
 3' -UUGUGACUAAAGUUUACCACGAU-5' miR-29b-3p SEQ ID NO: 13

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

FIG. 20B

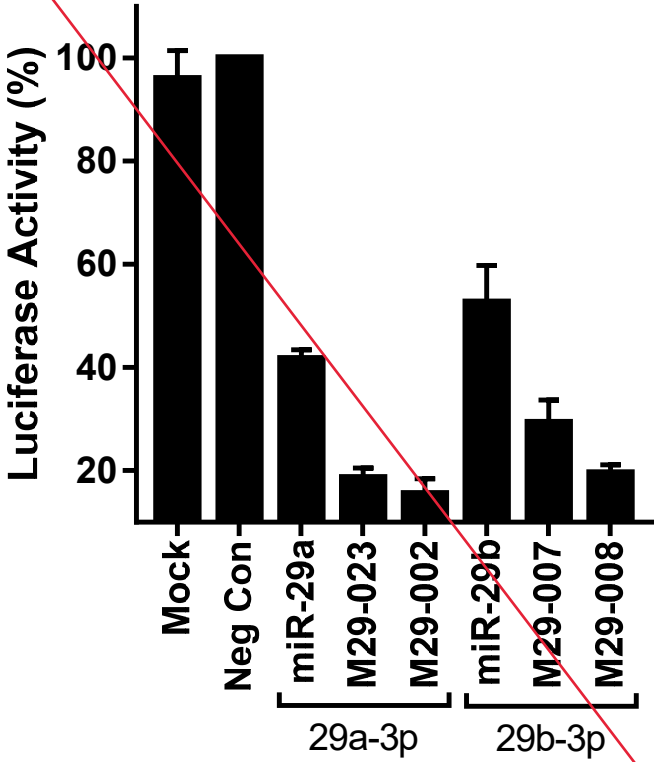


FIG. 20C

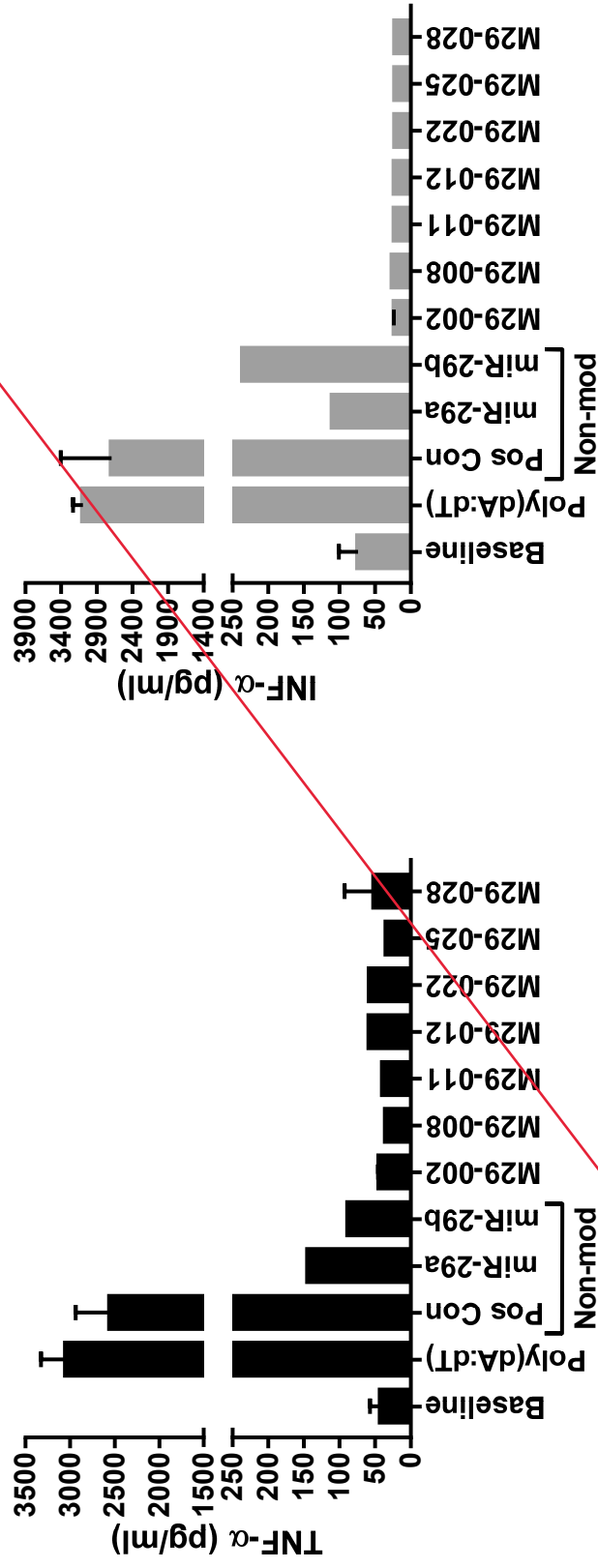


FIG. 21

FIG. 22A

<div><div>HIV-1 NEF site:</div><div>miR-29b-3p:</div></div>		<div>UC CC</div> <div>5' - CACUGA UUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGACU -AAGUUUACCACGAU -5' SEQ ID NO: 13</div> <div>UU A</div>	<div>UC CC</div> <div>5' - CACUGA UUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGACU -AAGUCUACCACGAU -5' SEQ ID NO: 102</div> <div>UU A</div>
<div>ΔG = -29.9 kcal/mol</div>		<div>ΔG = -32.6 kcal/mol</div>	
<div><div>HIV-1 NEF site:</div><div>G004-29:</div></div>		<div>UC C</div> <div>5' - CACUGA CUUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGACU -GAAGUUUACCACGAU -5' SEQ ID NO: 103</div> <div>UU</div>	<div>UC A</div> <div>5' - CACUG CCUUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGAC -GGAAGUUUACCACGAU -5' SEQ ID NO: 121</div> <div>UU</div>
<div>ΔG = -33.6 kcal/mol</div>		<div>ΔG = -35.7 kcal/mol</div>	
<div><div>HIV-1 NEF site:</div><div>G027-29:</div></div>		<div>UC</div> <div>5' - CACUGACCUUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGACUGGAAGUUUACCACGAU -5' SEQ ID NO: 117</div> <div>UU</div>	<div>UC</div> <div>5' - CACUGACCUUUGGAUGGUGCUA -3' SEQ ID NO: 470</div> <div> ::: </div> <div>3' - GUGACUGGAAGUUUACCACGAU -5' SEQ ID NO: 110</div> <div>UU</div>
<div>ΔG = -40.6 kcal/mol</div>		<div>ΔG = -43.4 kcal/mol</div>	

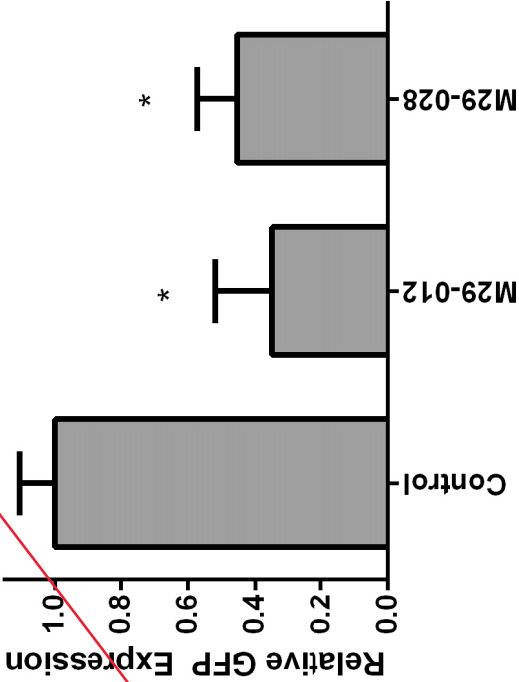


FIG. 22B

FIG. 23A

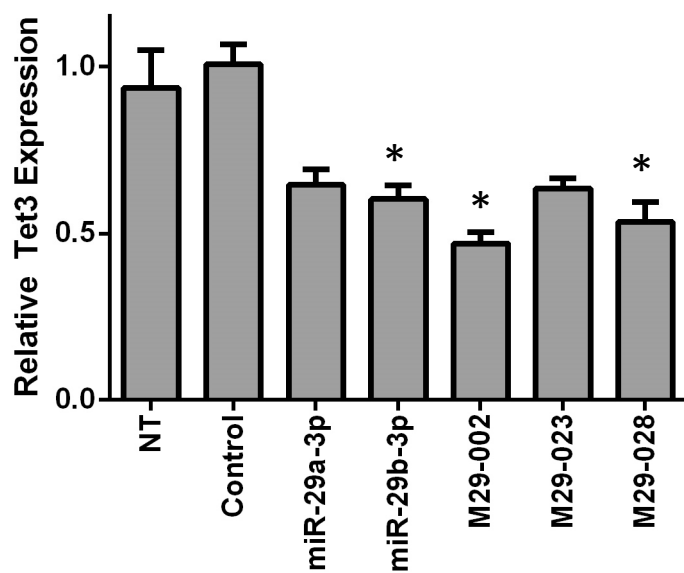


FIG. 23B

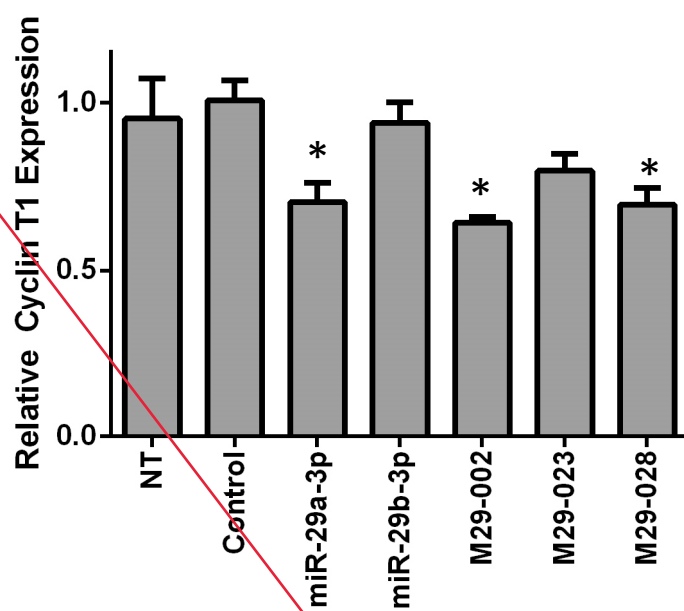
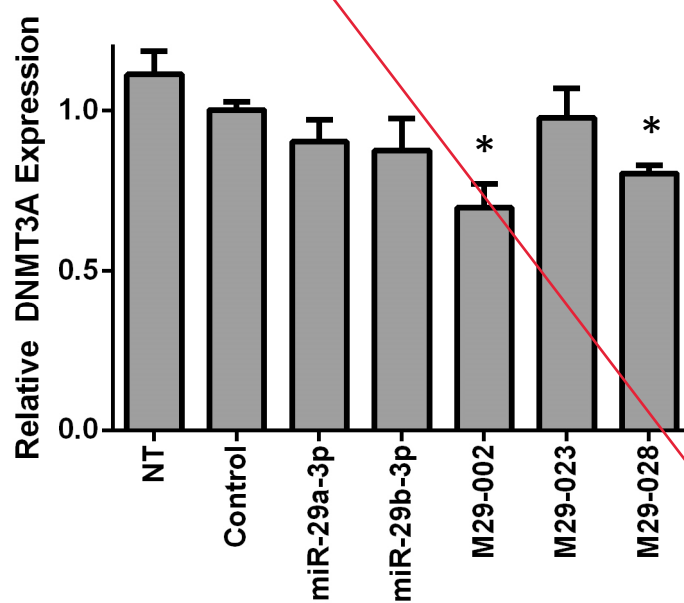


FIG. 23C



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

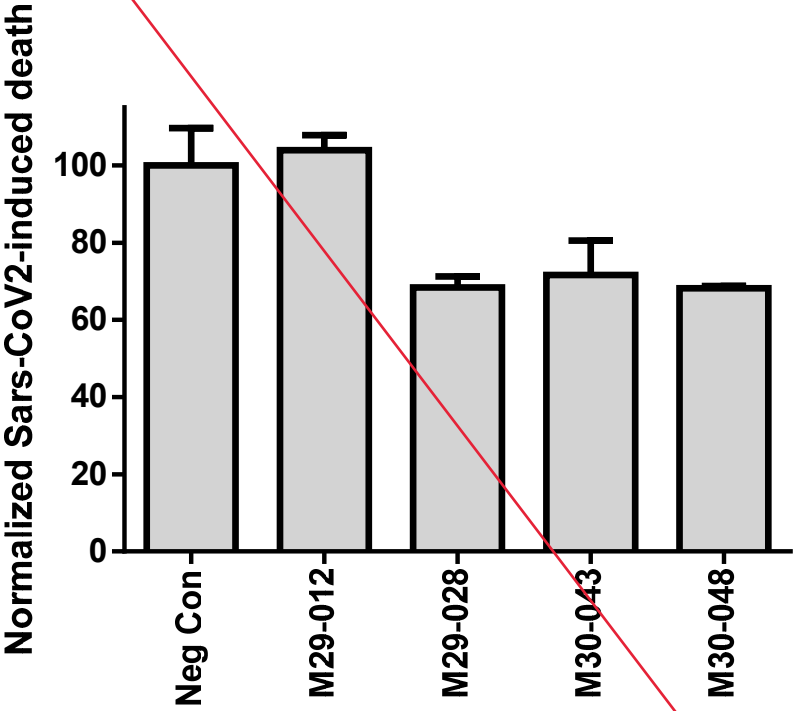


FIG. 25C

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

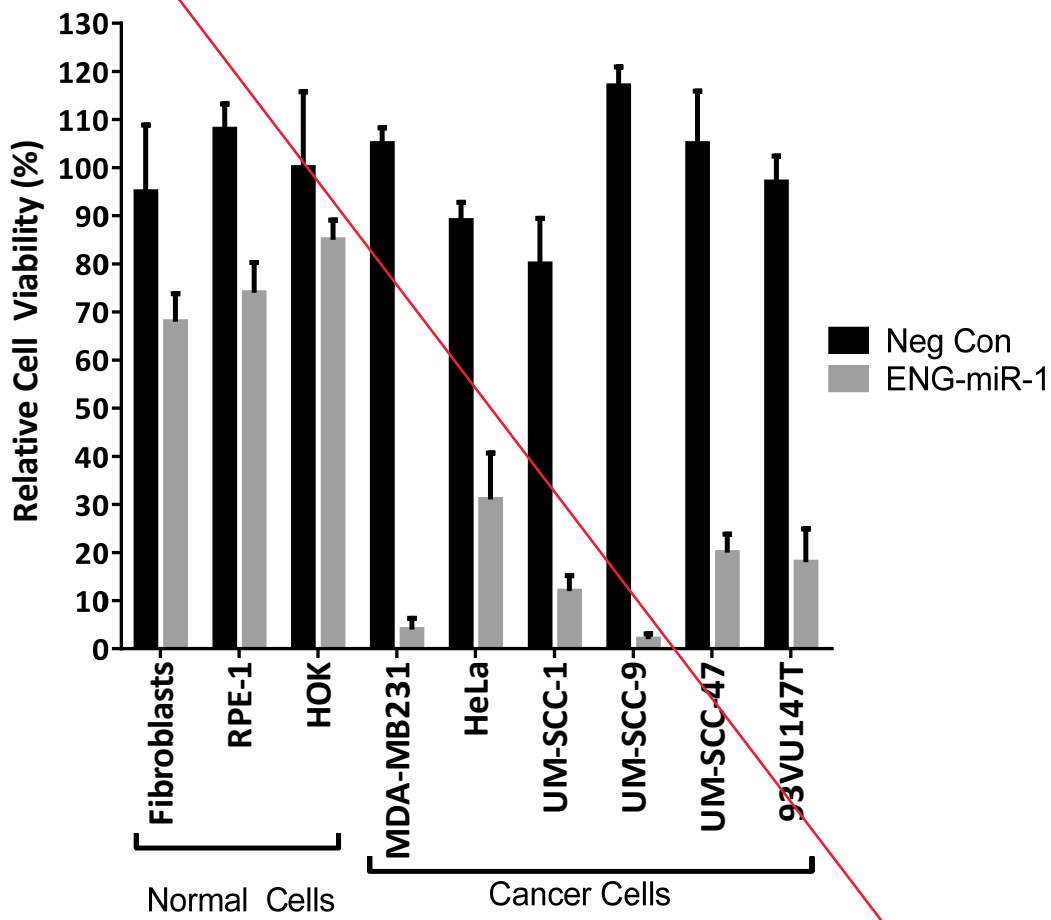


FIG. 27

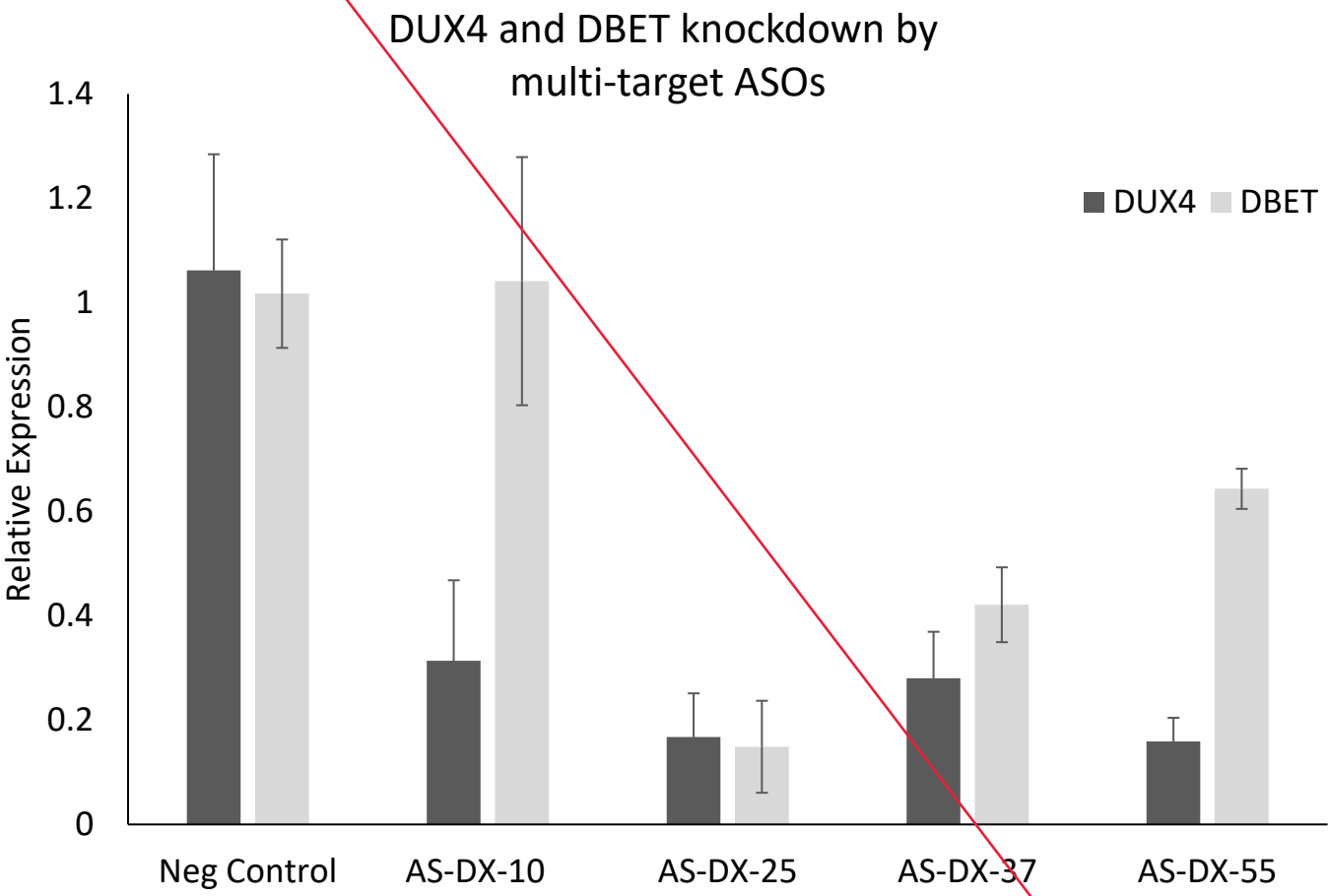


FIG. 28

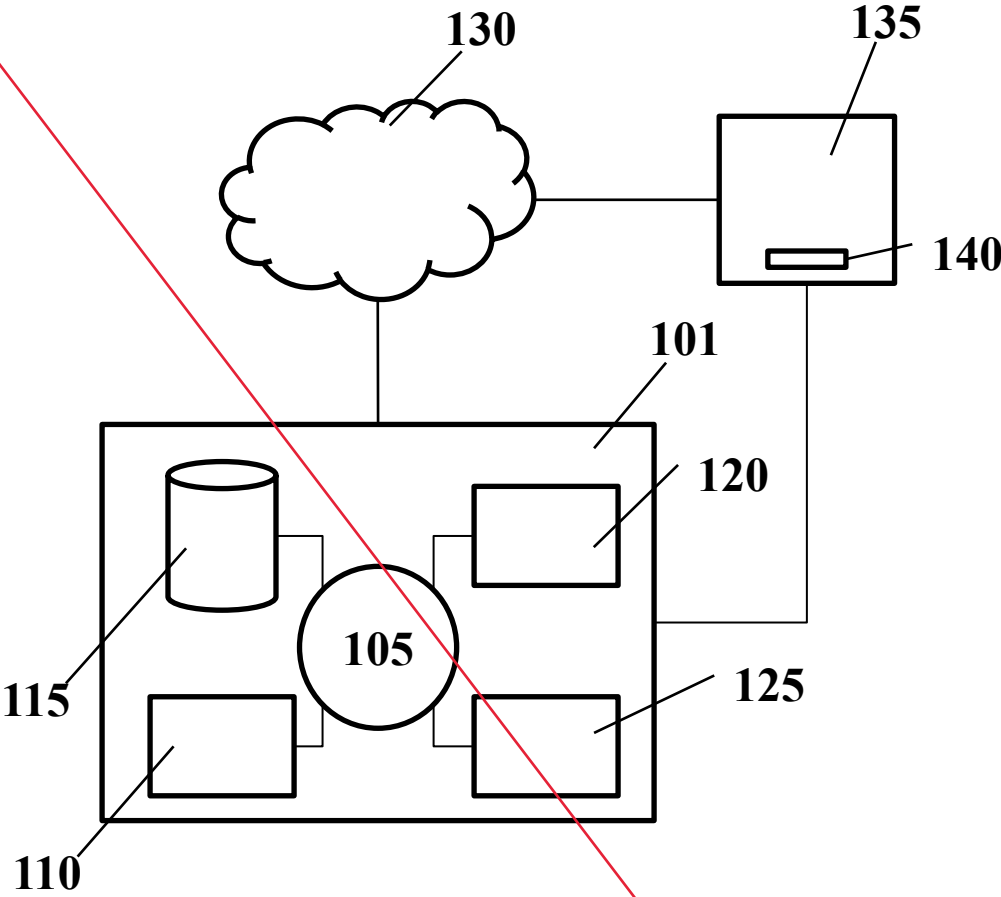


FIG. 29

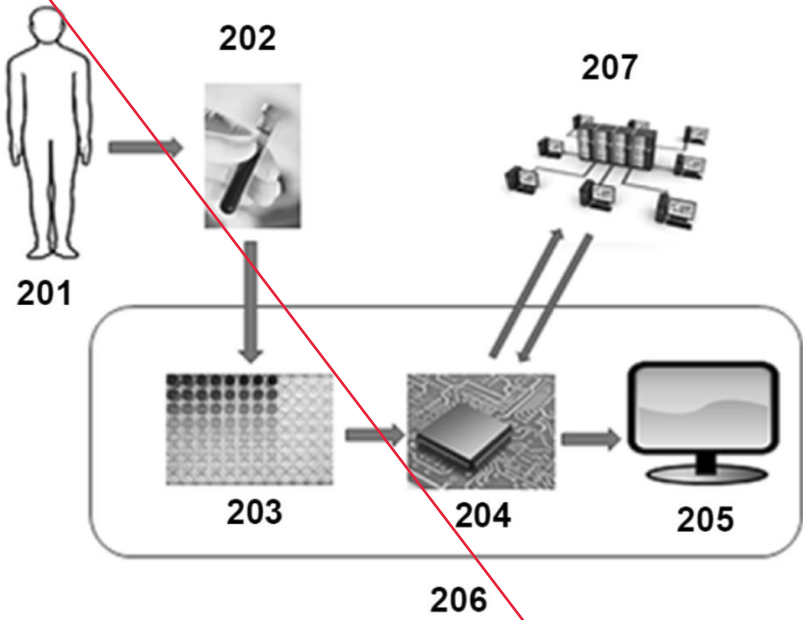


FIG. 30

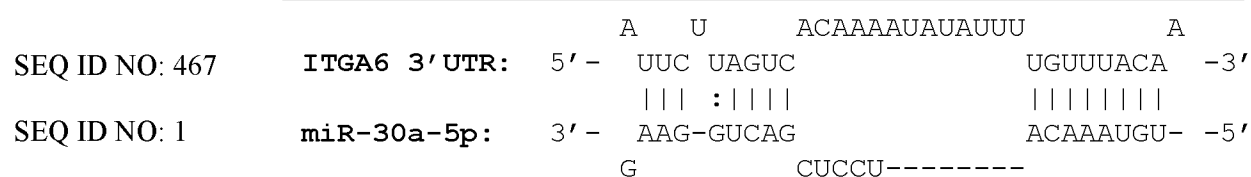
<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 1	miR-30a-5p	UGUAAACAUCCU-CGACUGGAAG
SEQ ID NO: 2	miR-30b-5p	UGUAAACAUCCU-ACACUC--AGCU
SEQ ID NO: 3	miR-30c-5p	UGUAAACAUCCU-ACACUCUCAGC
SEQ ID NO: 4	miR-30d-5p	UGUAAACAUCCC-CGACUGGAAG
SEQ ID NO: 5	miR-30e-5p	UGUAAACAUCCU-UGACUGGAAG
SEQ ID NO: 39	G007-30	UGUAAACAUCCU-CGACUGGAAG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

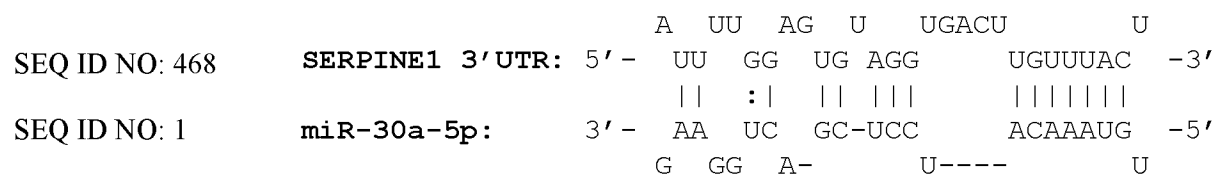
<u>Sequence (5' -> 3')</u>		
SEQ ID NO: 6	* miR-30a-3p	CUUUCAGUC---GGAUGUUUGCAGC
SEQ ID NO: 51	P125-30	--UUCAGUC---GGAUGUUUGCAGC
SEQ ID NO: 50	P005-30	--UCCAGUC---GGAUGUUUACA--
SEQ ID NO: 48	P003-30	--UCCAGUCG-AGGAUGUUUACA--
SEQ ID NO: 49	P004-30	--UCCAGUCGCAGGAUGUUUACA--
SEQ ID NO: 47	P002-30	---CCAGUCGCAGGAUGUUUACA--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

*Natural

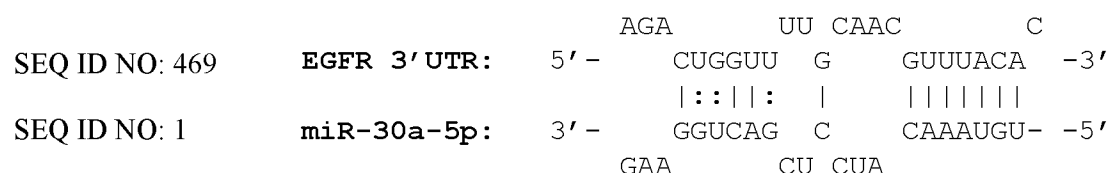
FIG. 1B



$$\Delta G = -17.4 \text{ kcal/mol}$$

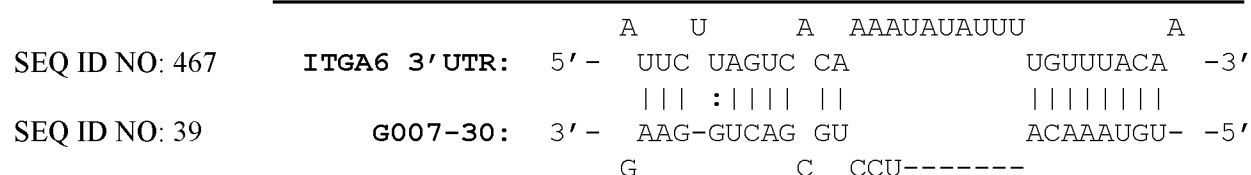


$$\Delta G = -17.5 \text{ kcal/mol}$$

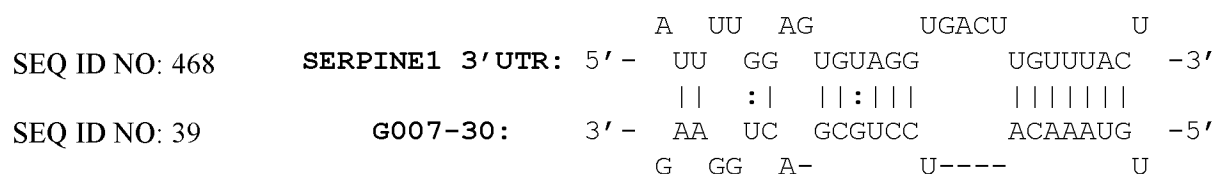


$$\Delta G = -15.5 \text{ kcal/mol}$$

FIG. 2A



$$\Delta G = -19.0 \text{ kcal/mol}$$



$$\Delta G = -22.4 \text{ kcal/mol}$$



$$\Delta G = -18.6 \text{ kcal/mol}$$

FIG. 2B

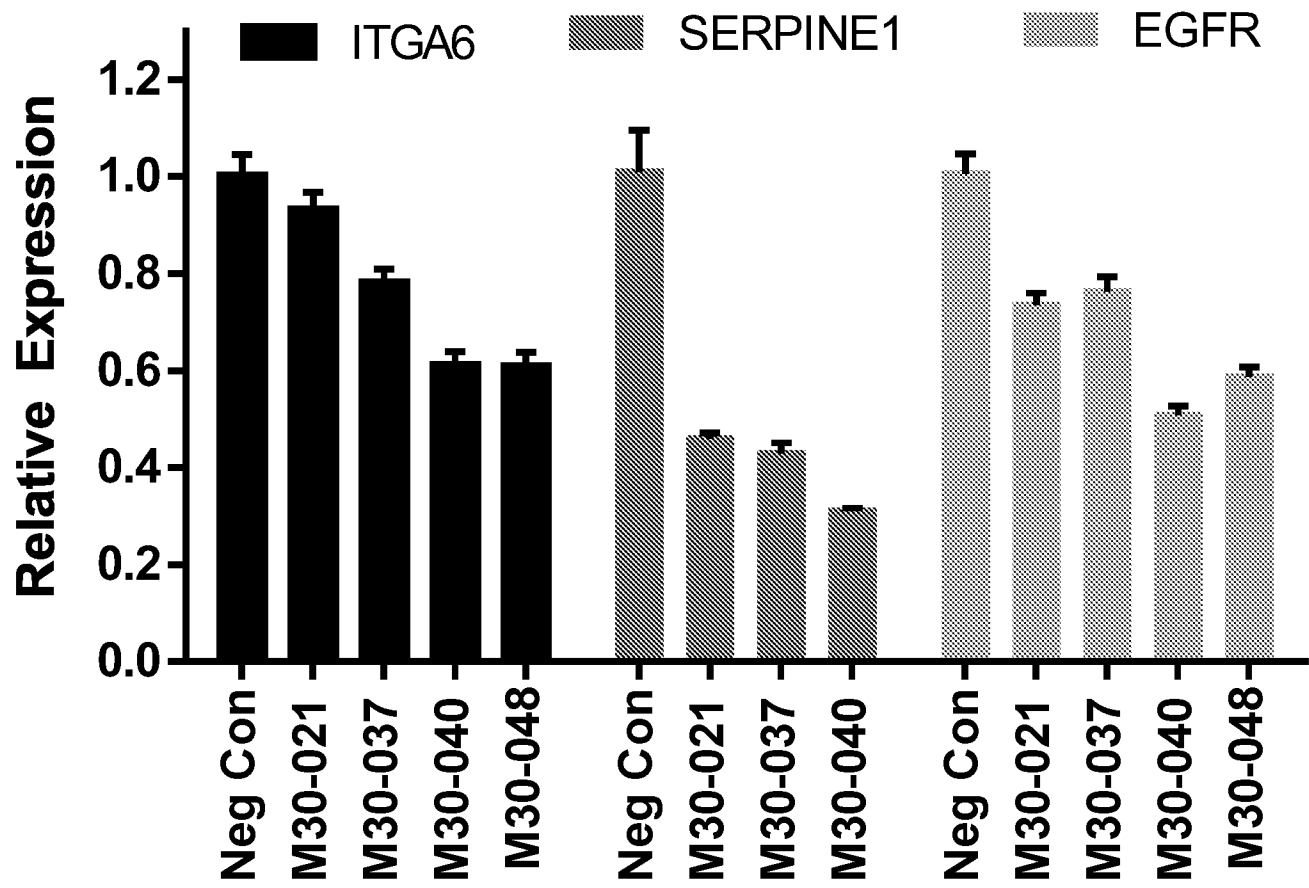
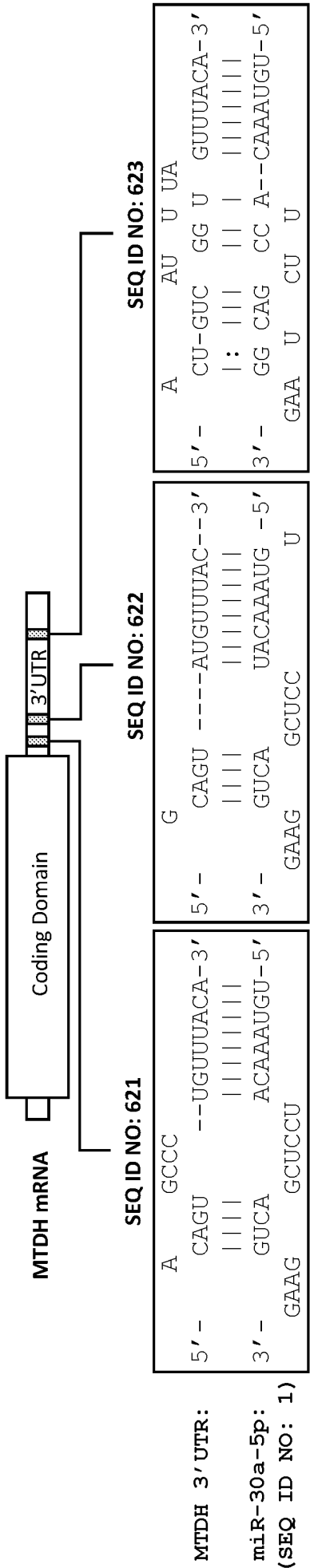


FIG. 2C



SEQ ID NO:	Strand	SEQ ID NO:			NET	Avg
1	miR-30a-5p	621	622	623	-46.5	-15.5
2	miR-30b-5p	-14.9	-13.9	-15.2	-44.0	-14.7
3	miR-30c-5p	-14.9	-14	-14.4	-43.3	-14.4
4	miR-30d-5p	-15.4	-14.6	-17	-47.0	-15.7
5	miR-30e-5p	-15.4	-14.6	-19.6	-49.6	-16.5
39	G007-30	-18.3	-19.4	-17.1	-54.8	-18.3
624	G075-30	-15.5	-16.3	-19.5	-51.3	-17.1
40	G061-30	-18.3	-15.6	-18.2	-52.1	-17.4
41	G062-30	-16.3	-17.9	-19.9	-54.1	-18.0
625	G076-30	-13.8	-17.1	-26.7	-57.6	-19.2
626	G077-30	-15.4	-19	-17.2	-51.6	-17.2
627	G078-30	-18.3	-19.5	-17.9	-55.7	-18.6

Hybridization Free Energy (kcal/mol)

FIG. 3

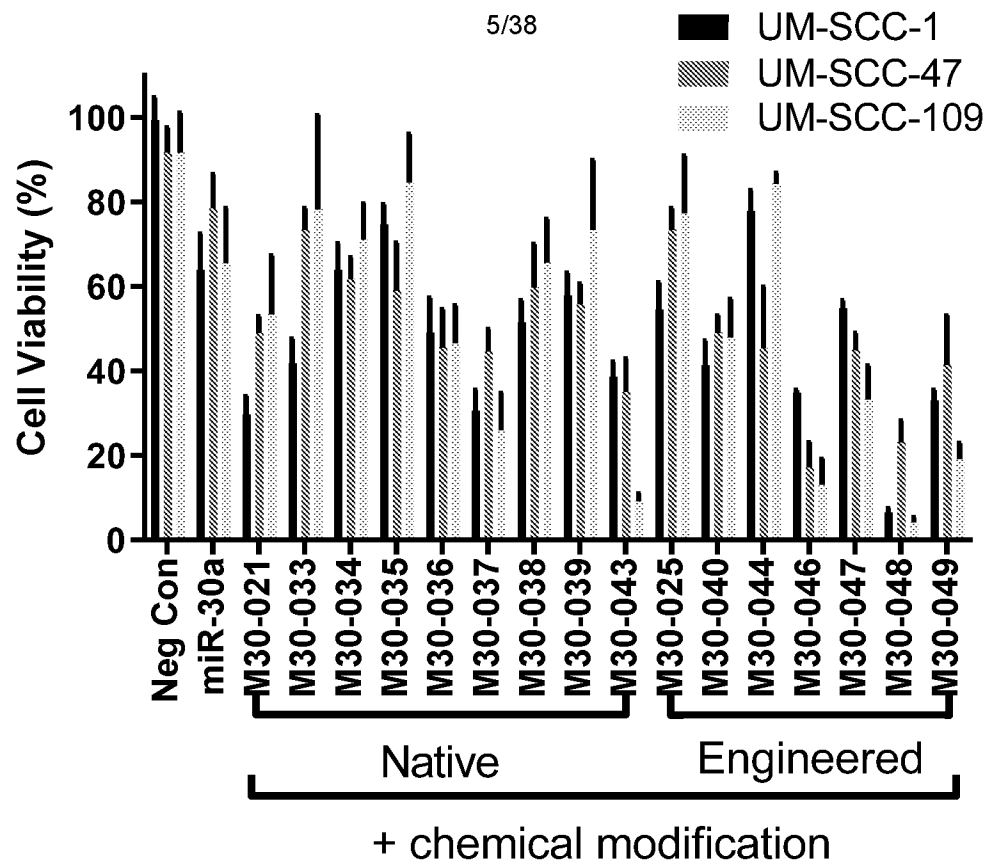


FIG. 4A

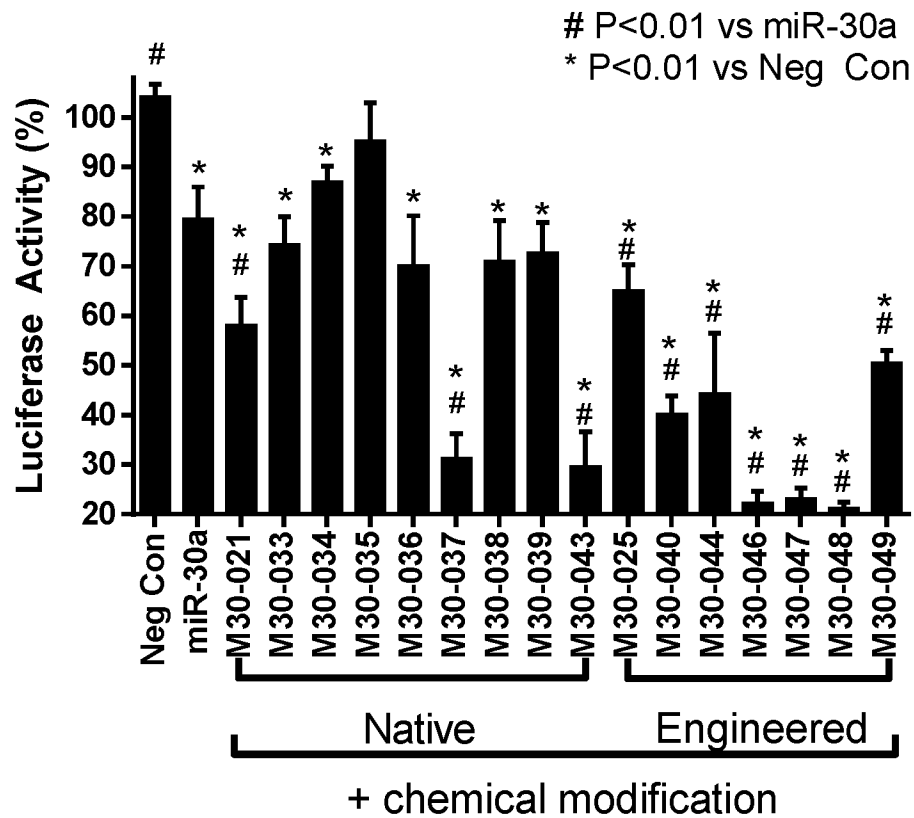


FIG. 4B

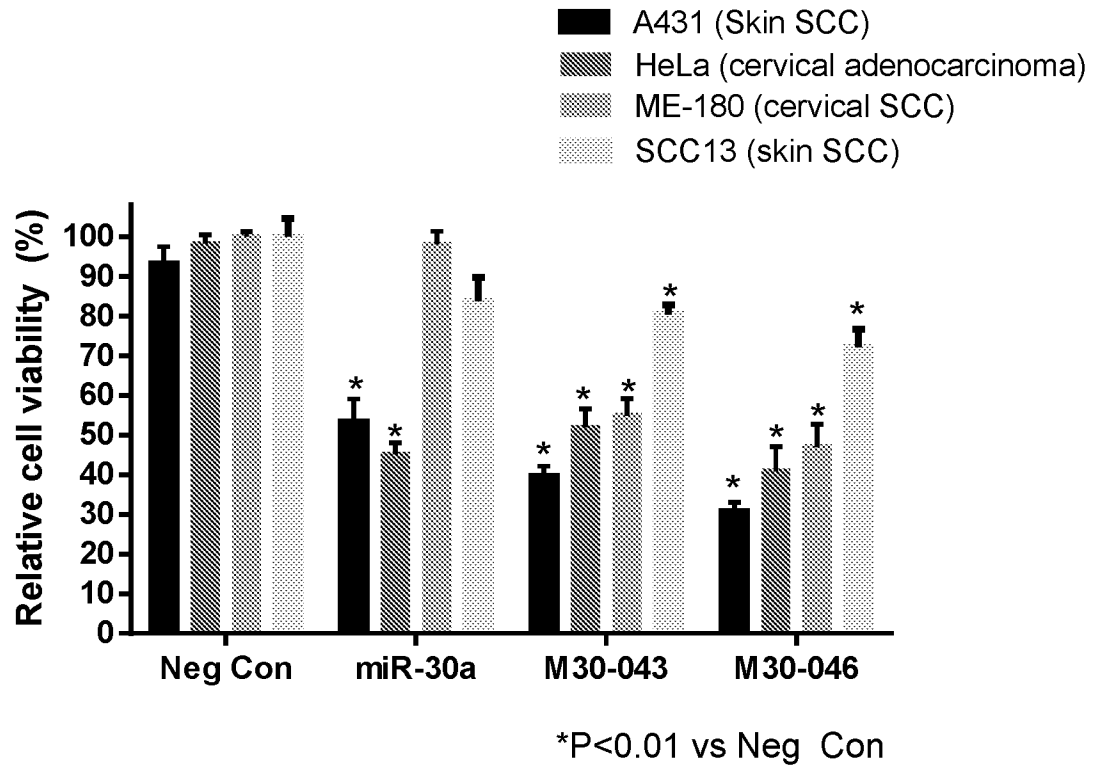


FIG. 4C

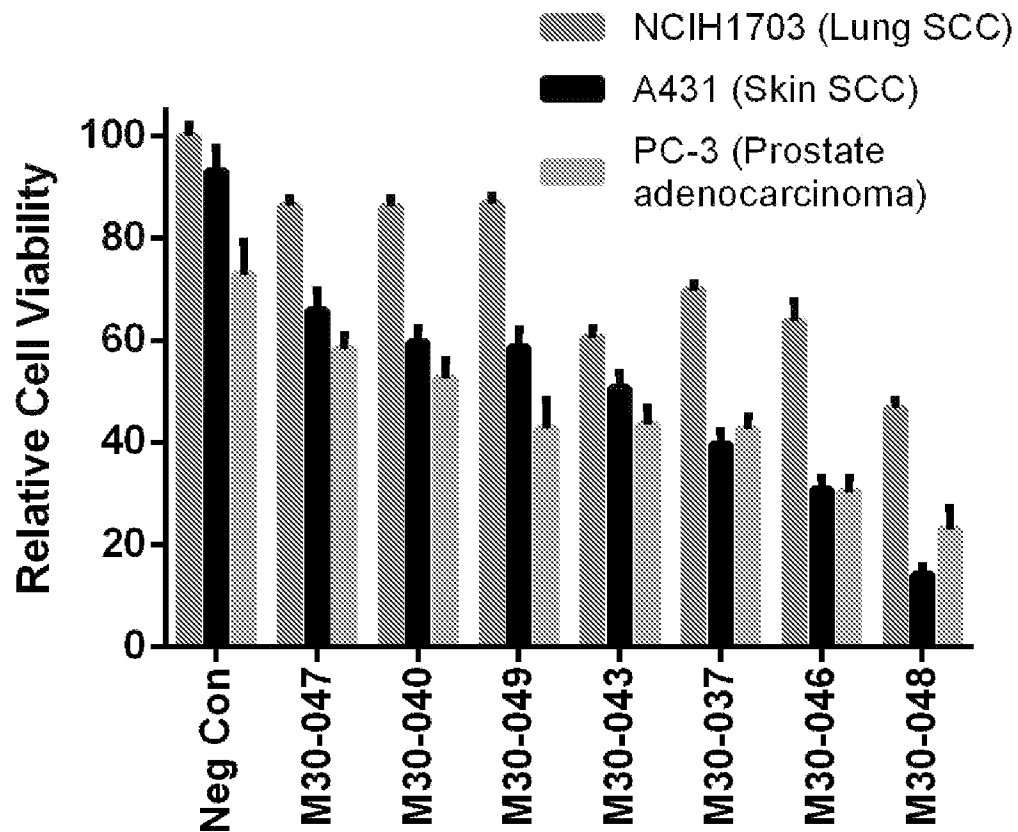


FIG. 4D

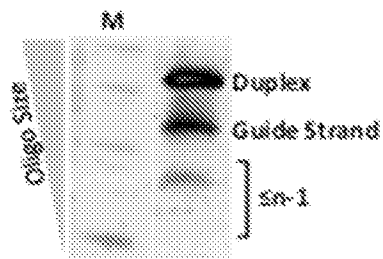


FIG. 5A

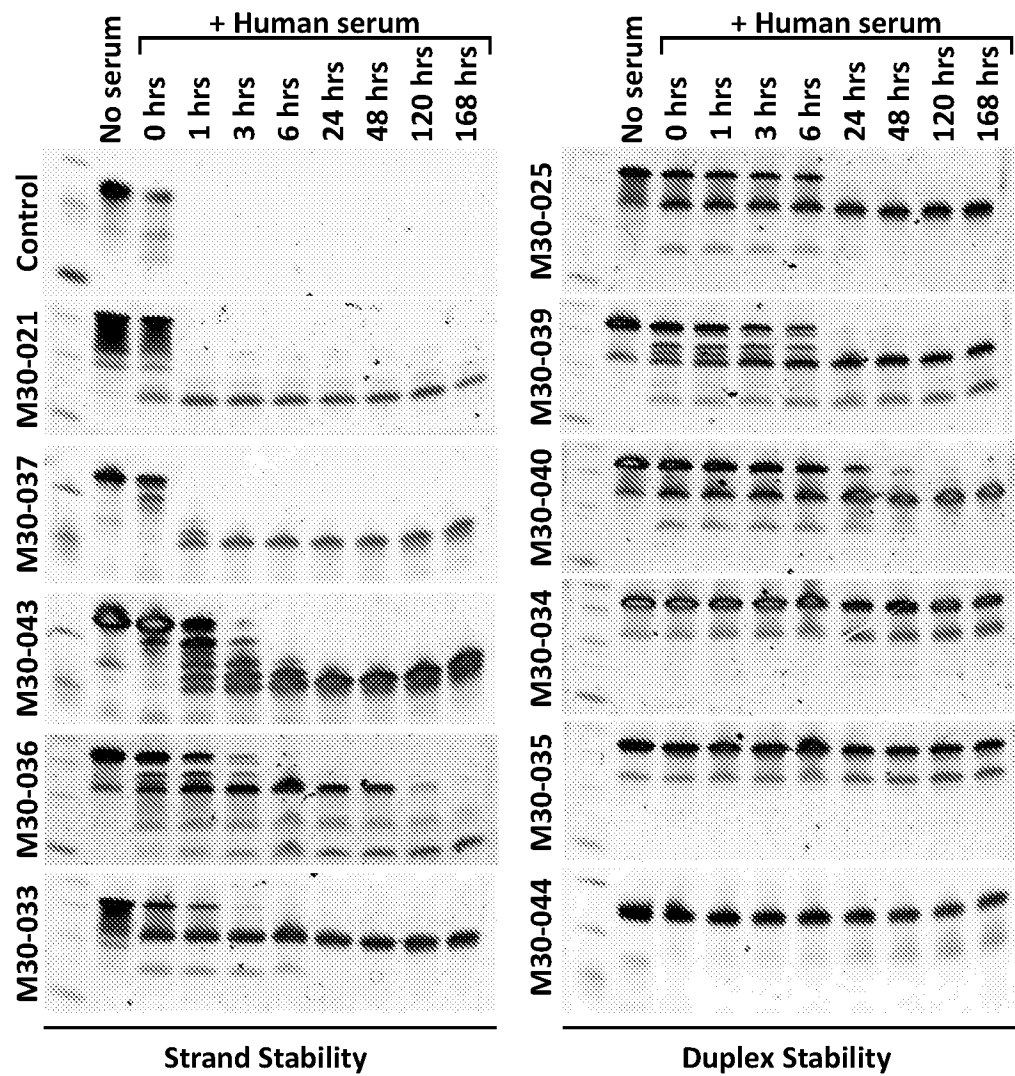


FIG. 5B

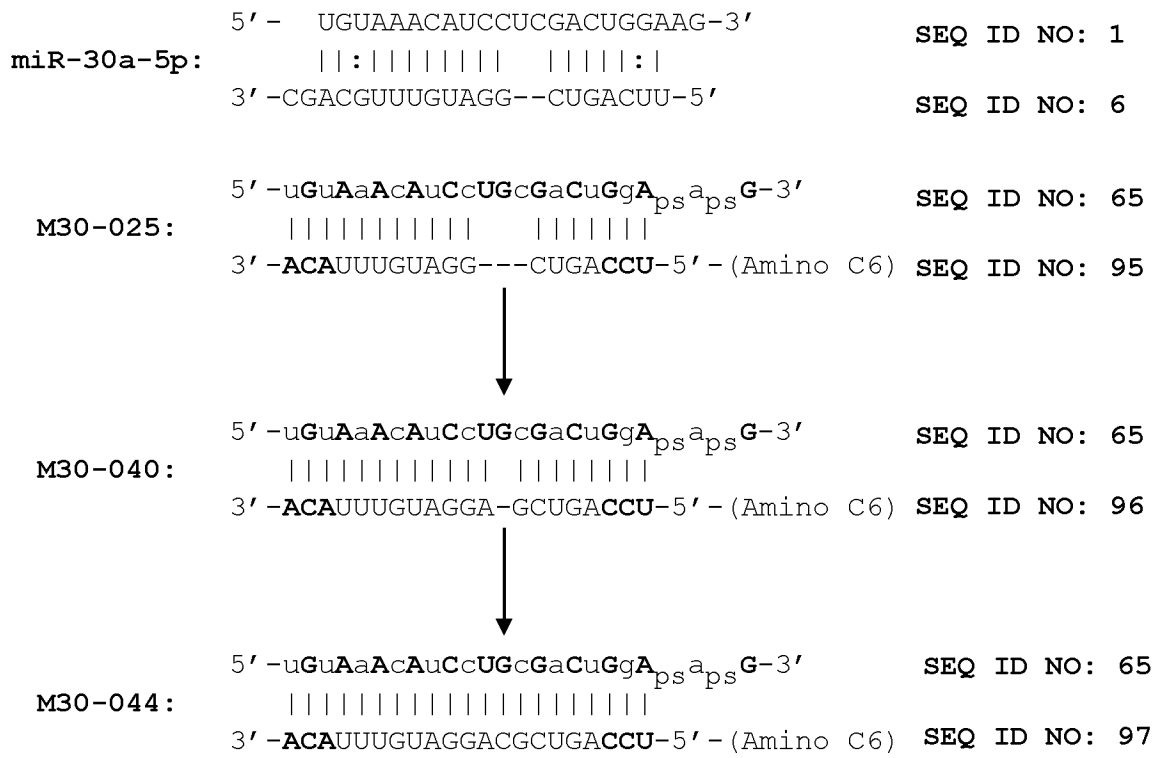


FIG. 6A

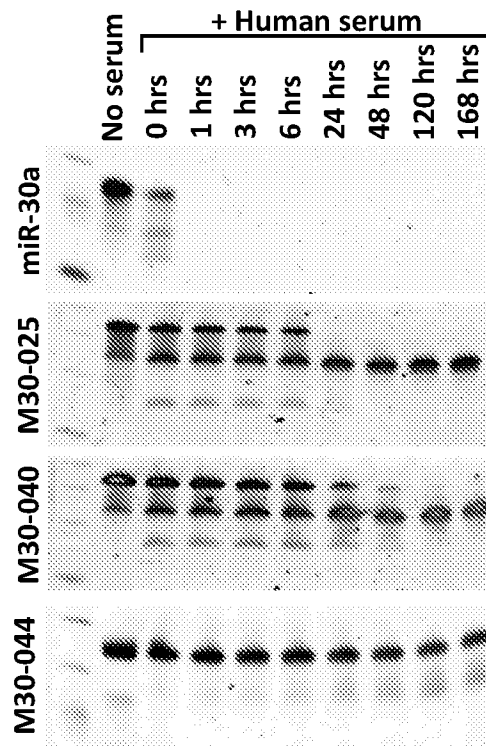
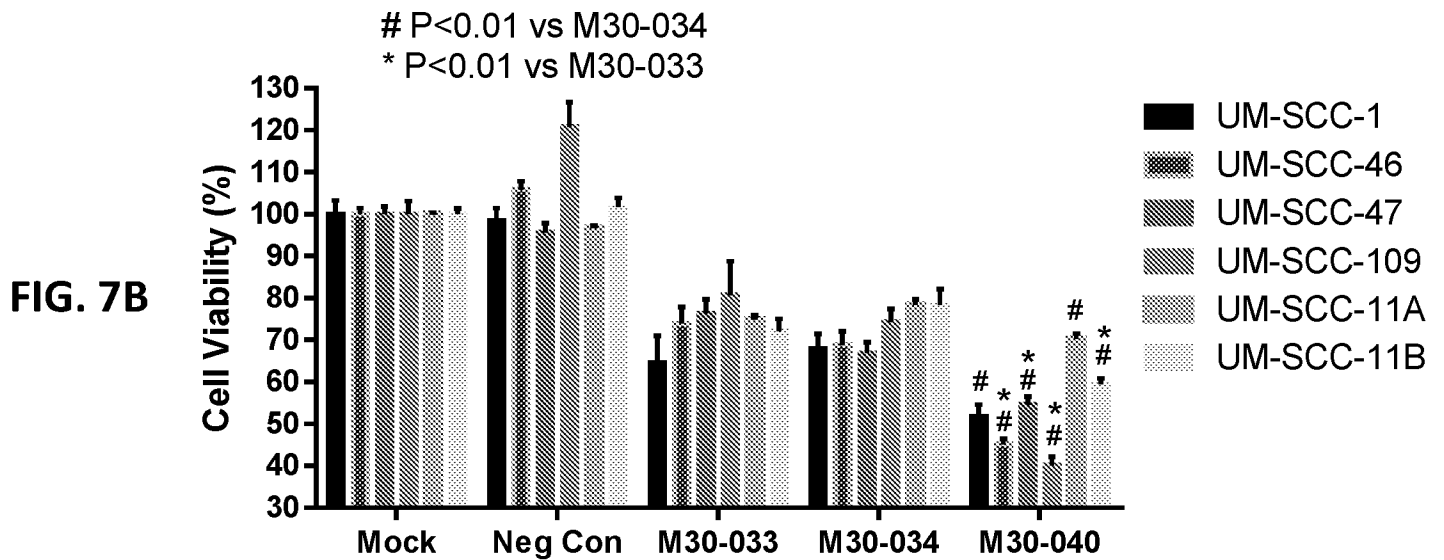
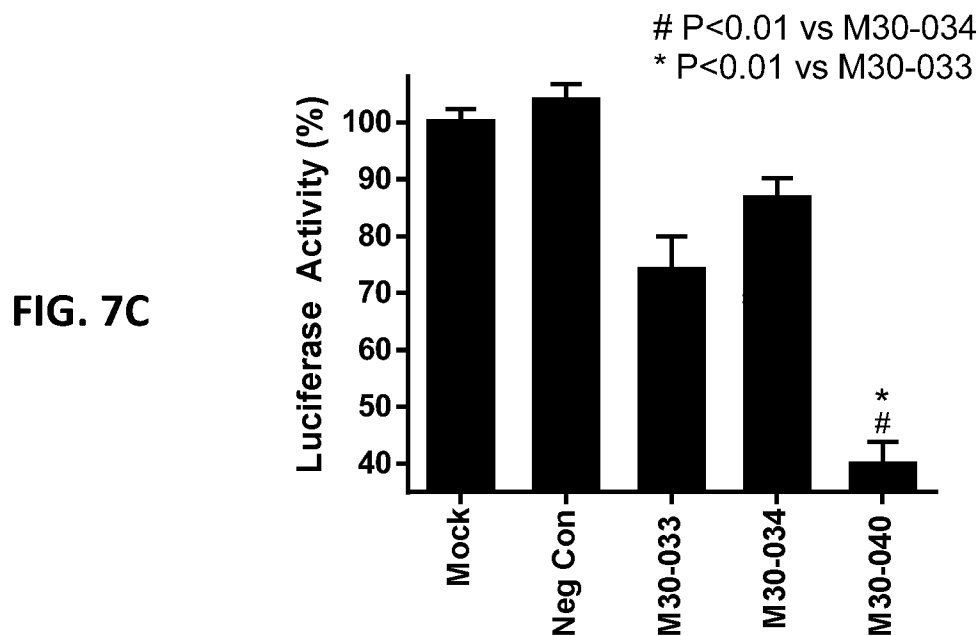
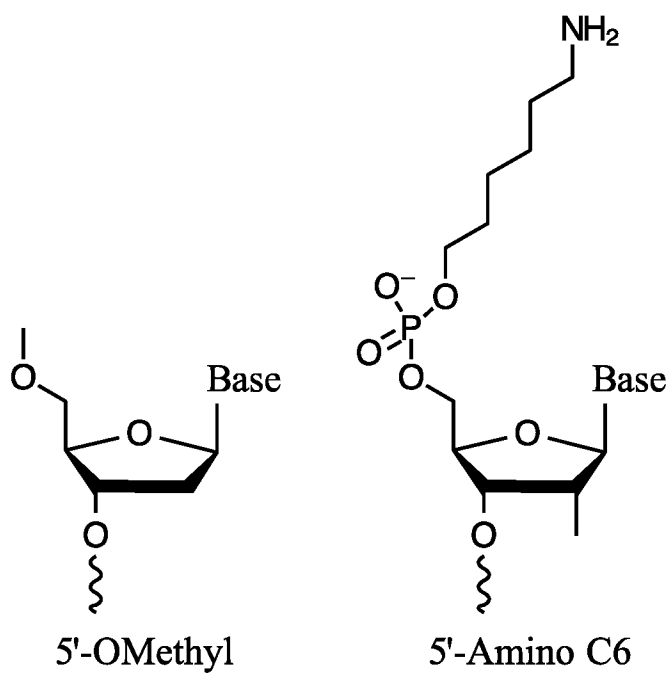
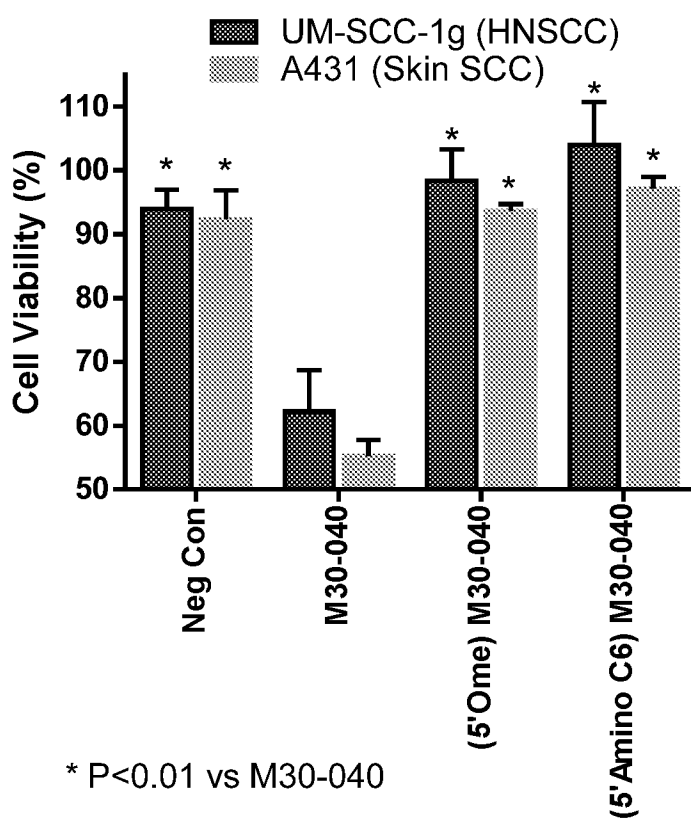


FIG. 6B

FIG. 7A



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

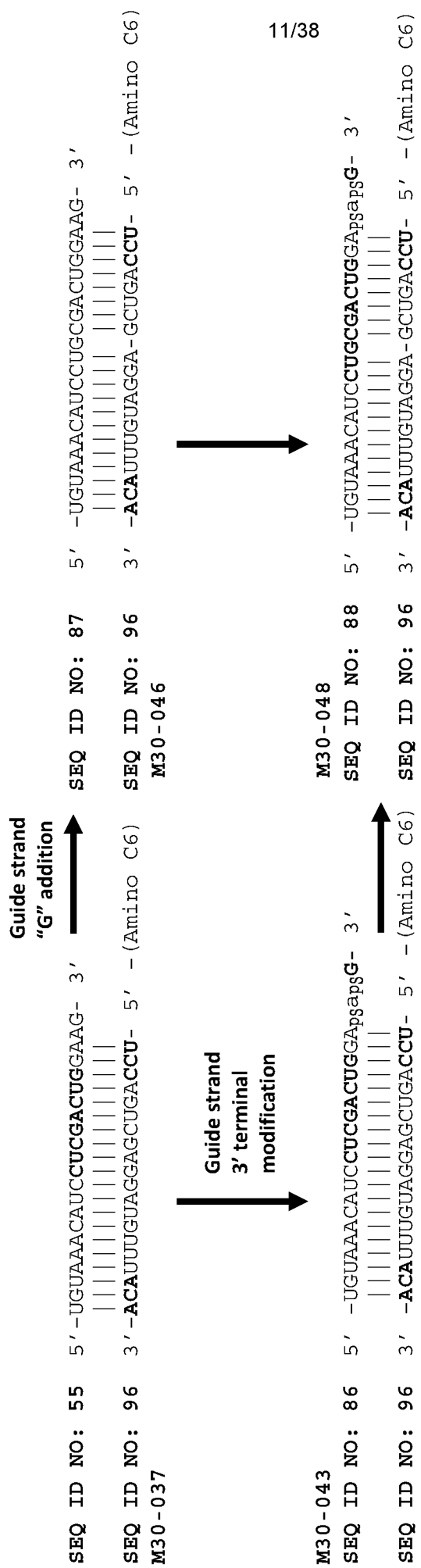


FIG. 9A

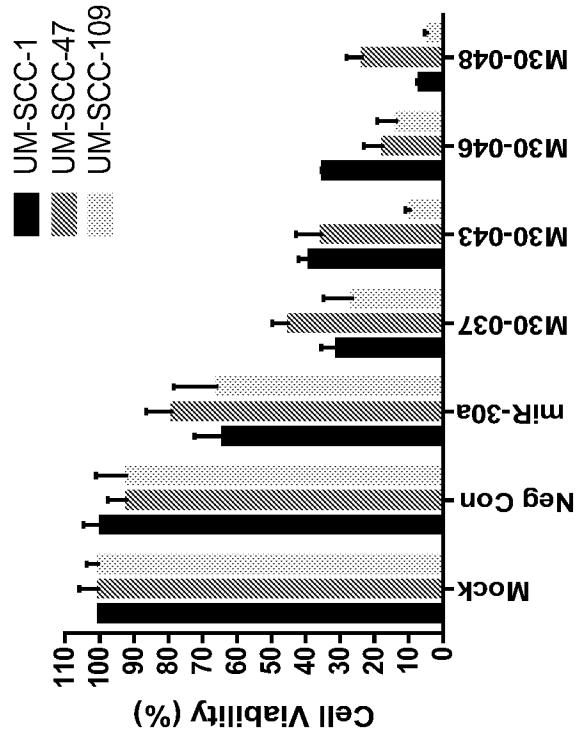


FIG. 9B

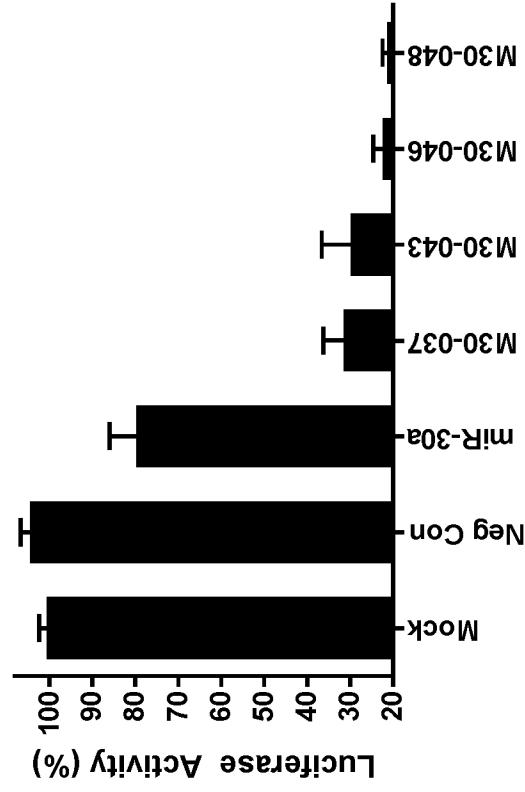


FIG. 9C

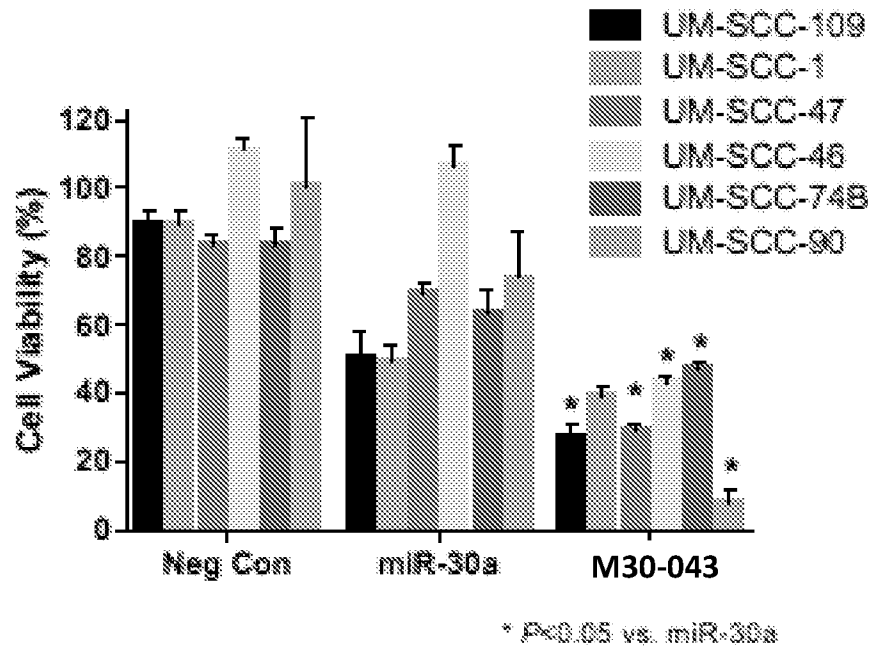


FIG. 10A

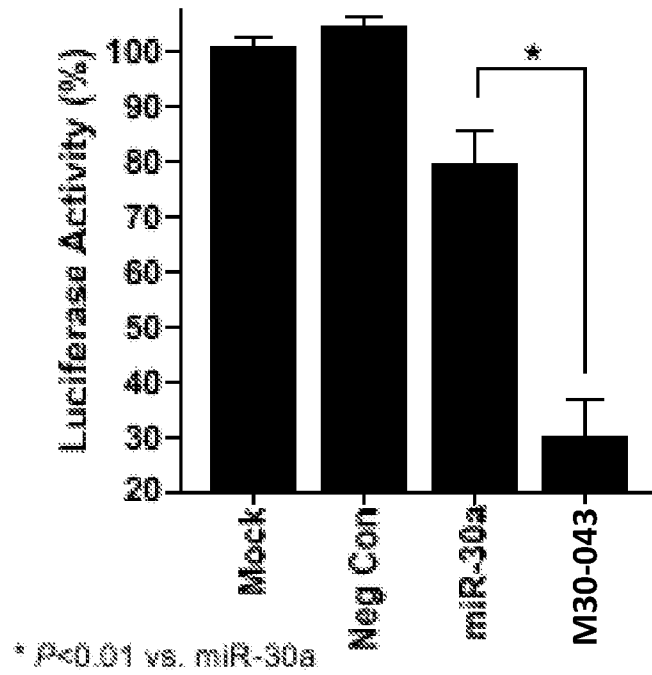


FIG. 10B

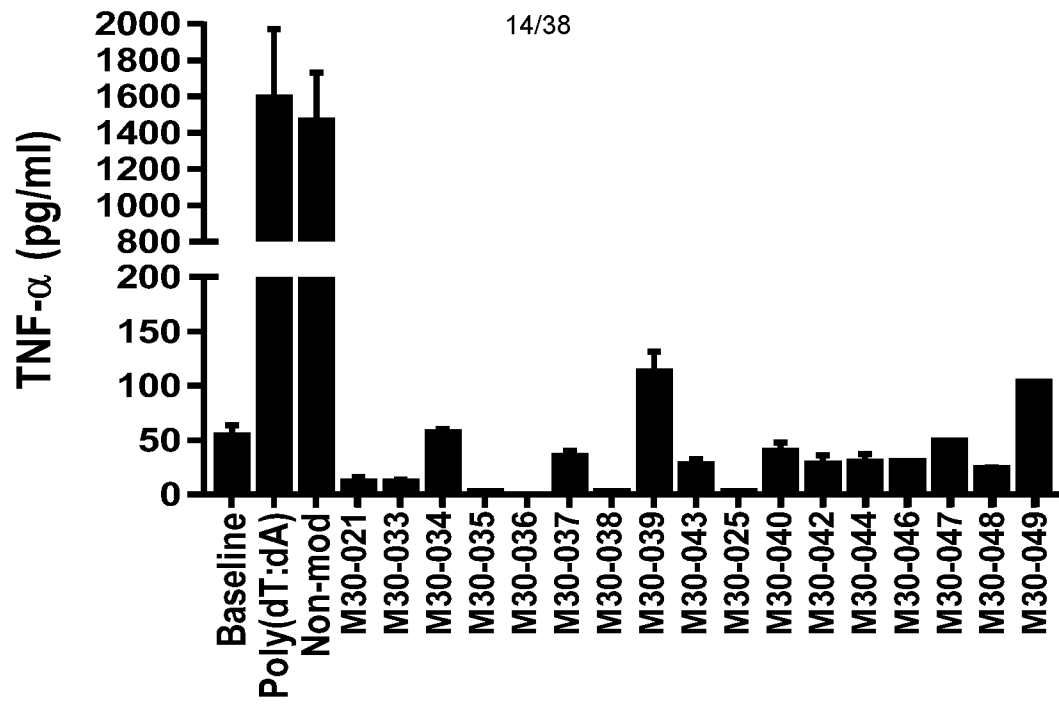


FIG. 11A

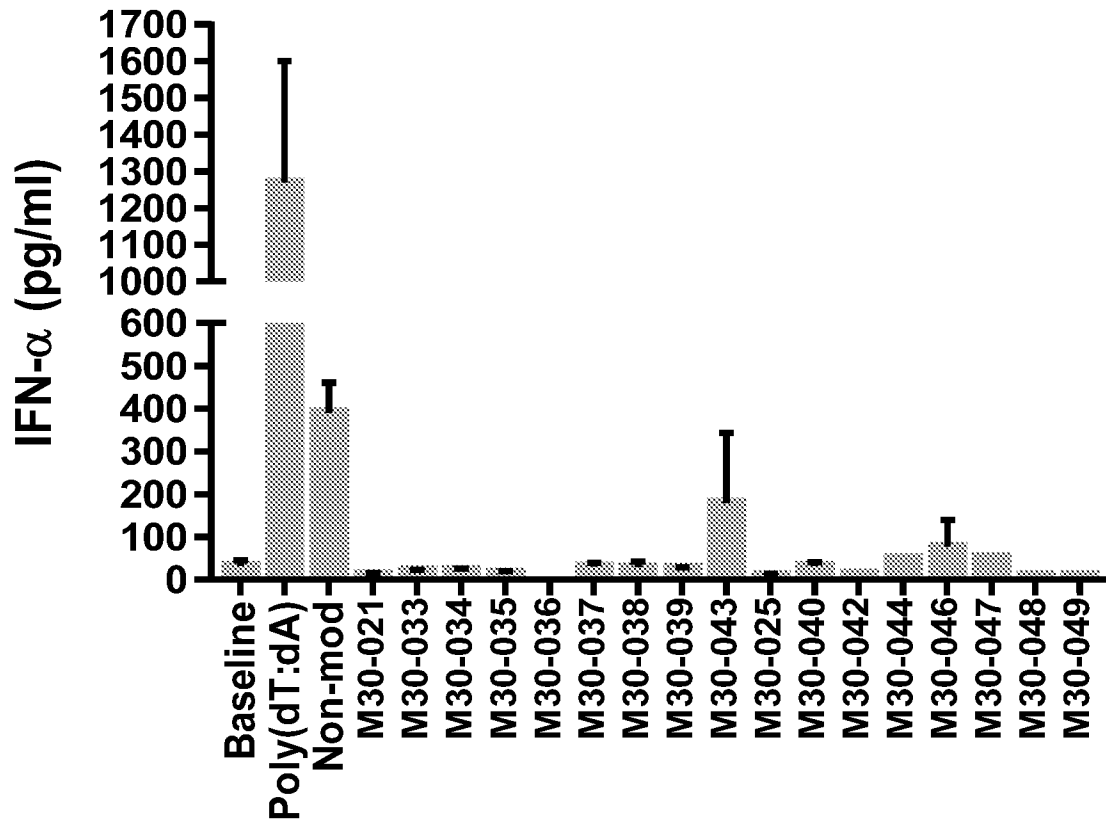


FIG. 11B

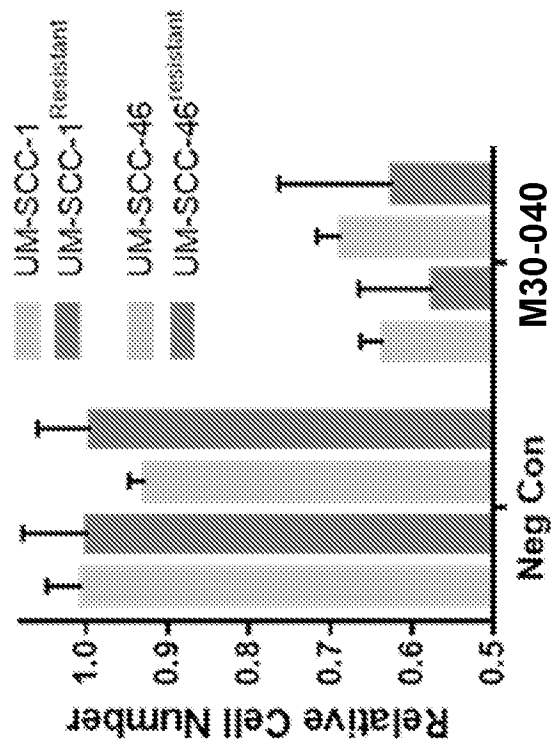


FIG. 12B

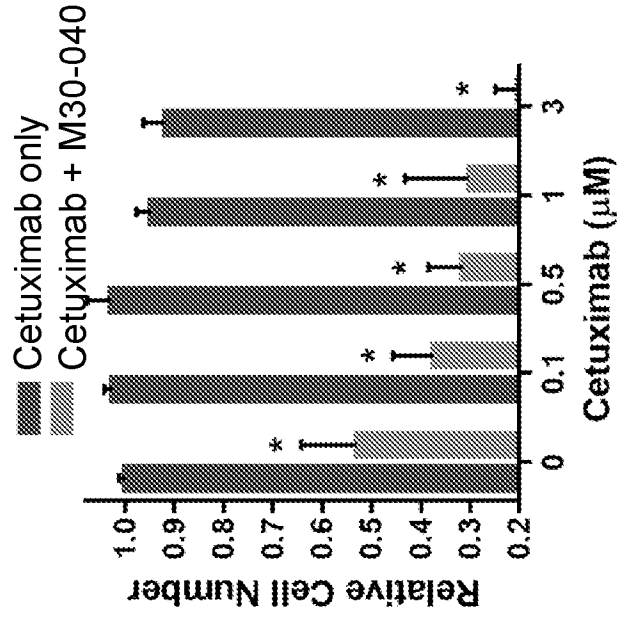


FIG. 12D

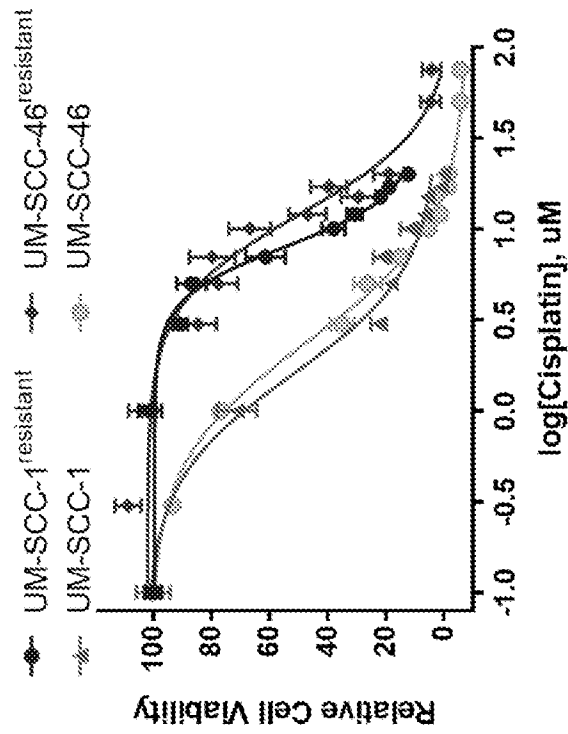


FIG. 12A

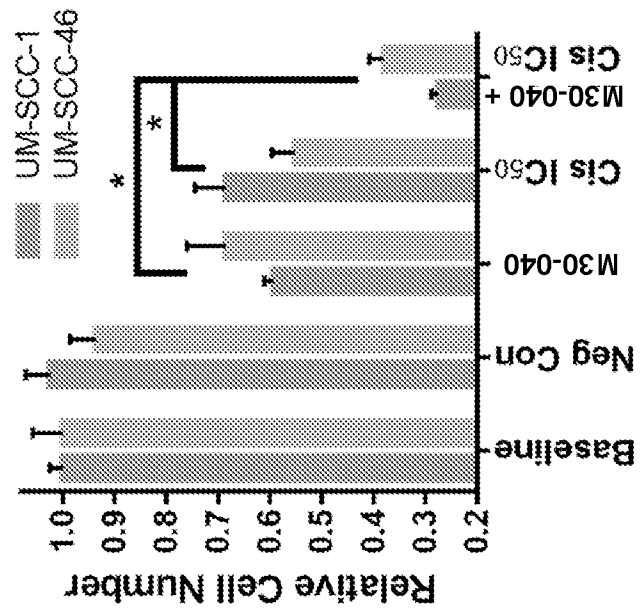
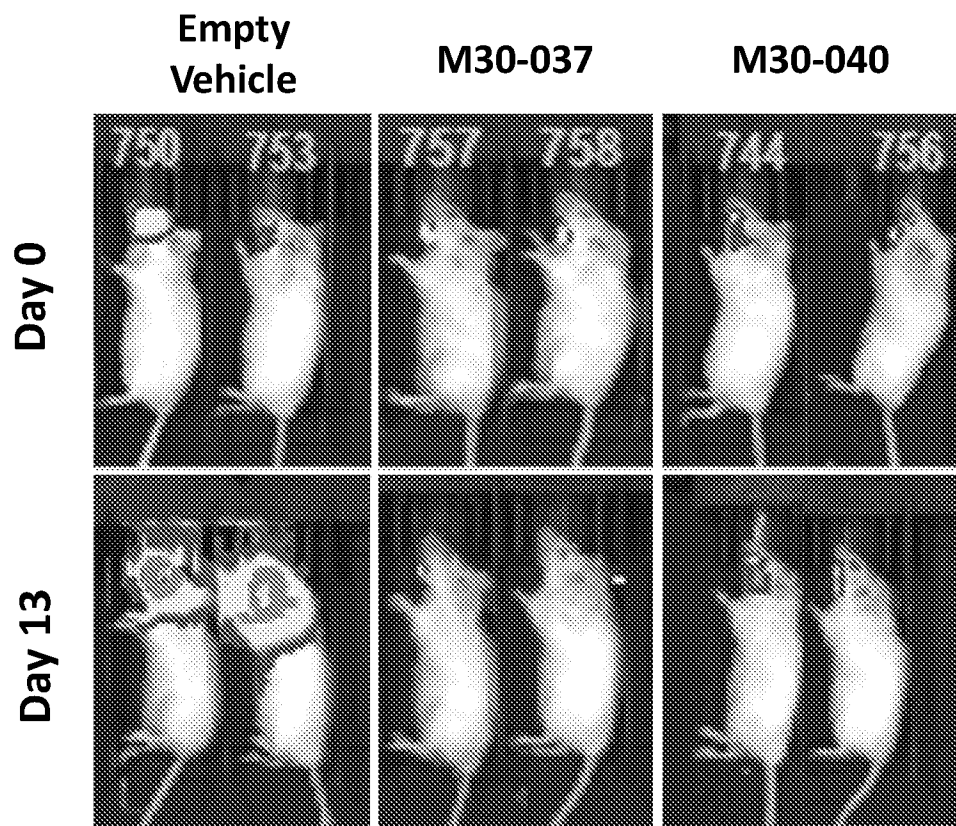
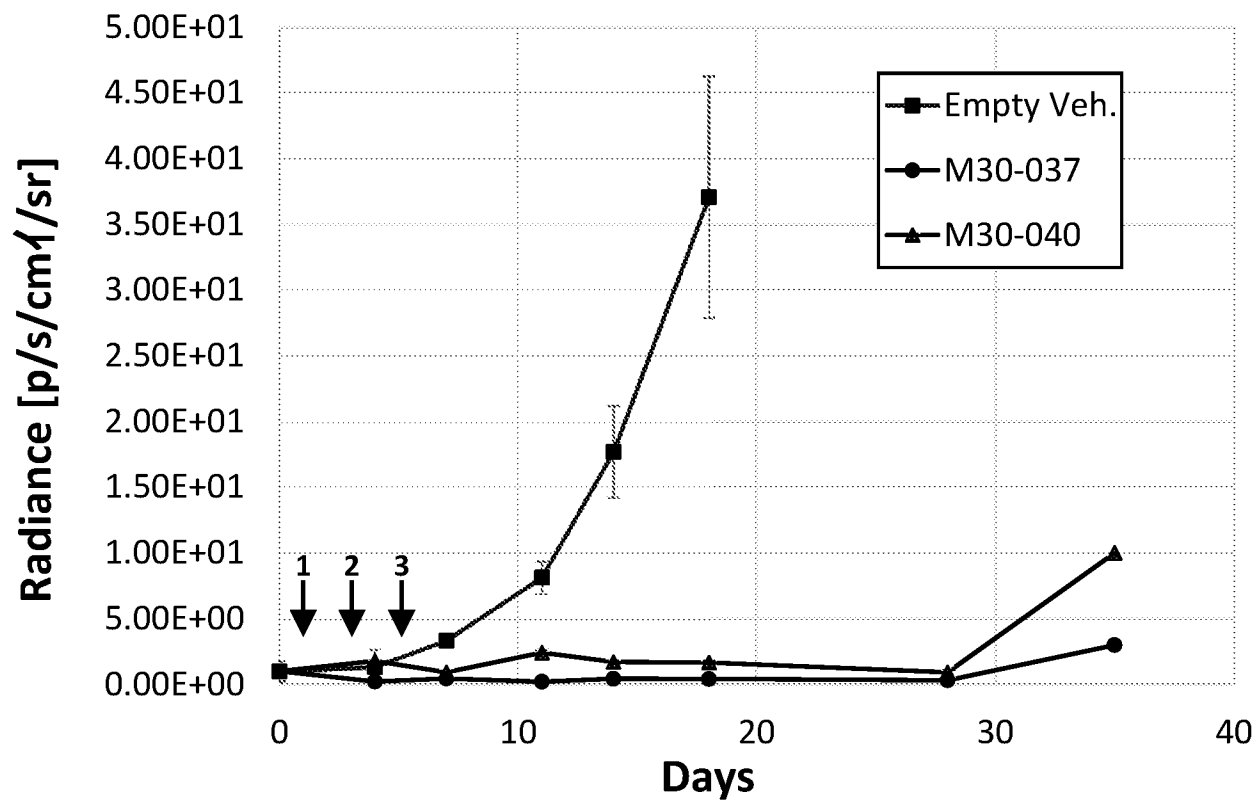
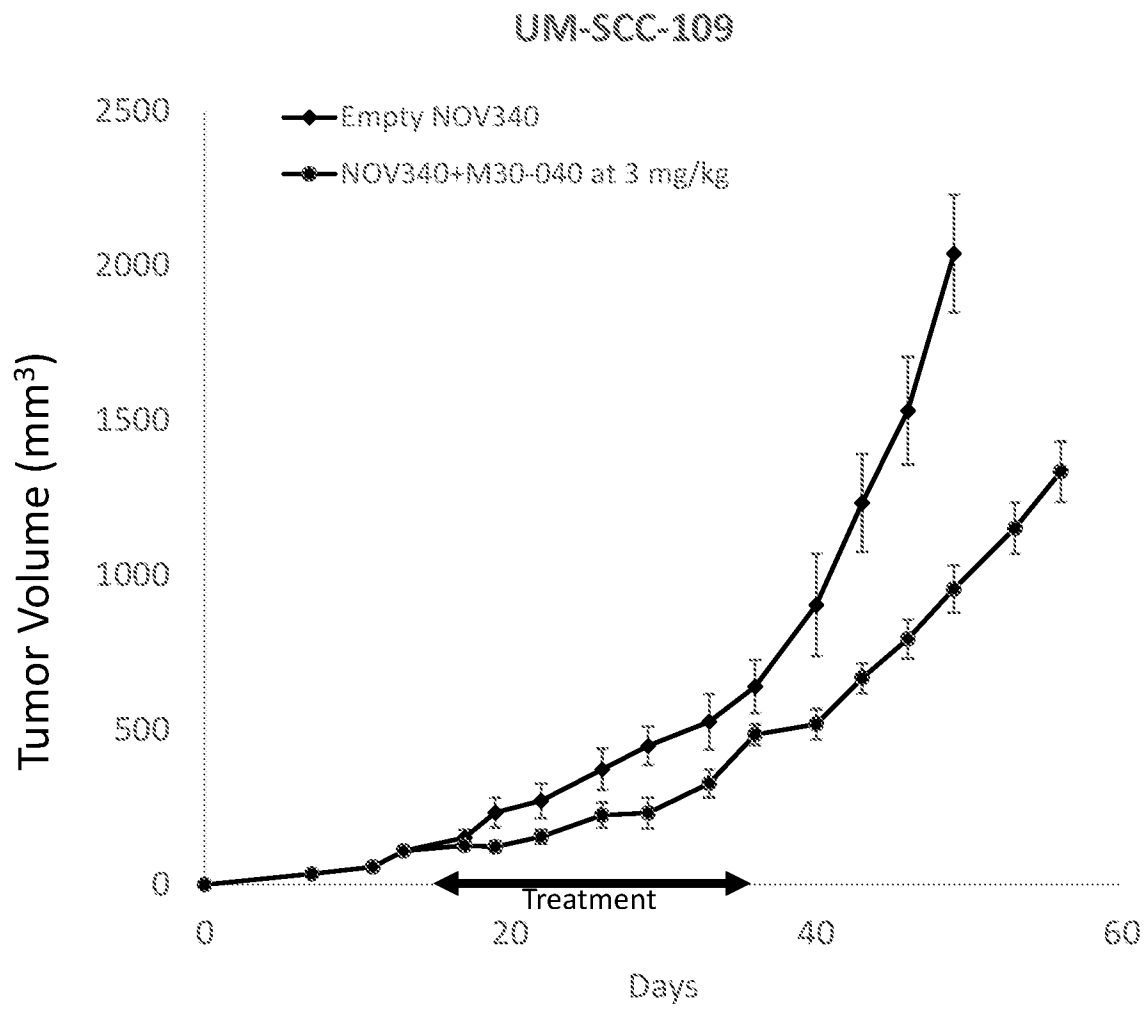


FIG. 12C

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

**FIG. 13C**

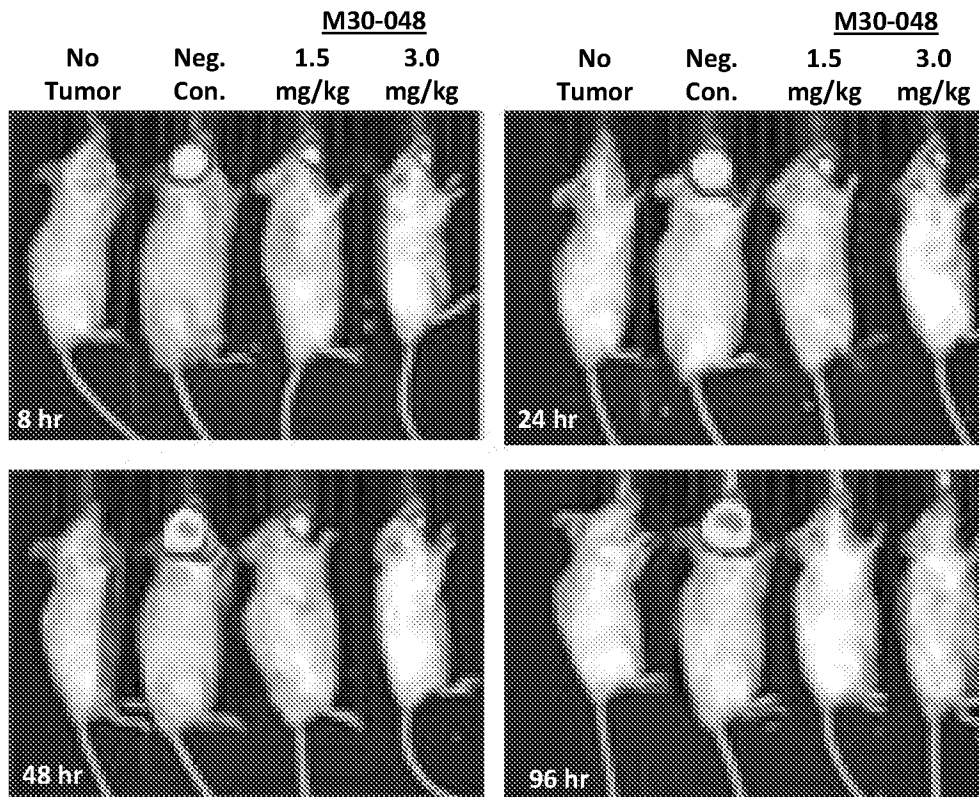


FIG. 14A

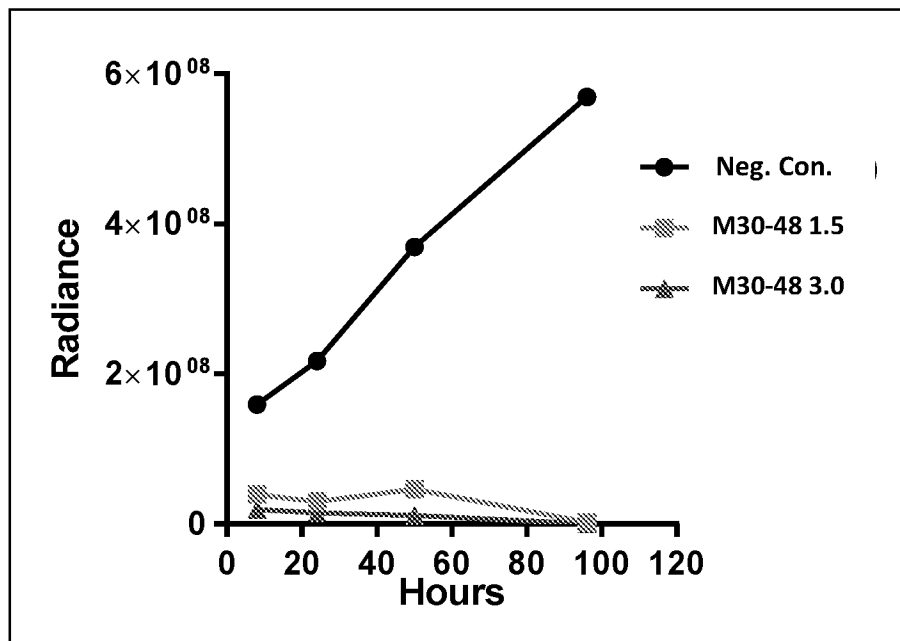


FIG. 14B

<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	Hybrid
SEQ ID NO: 101		G002-29 UAGCACCAUUGAAAUCAGUGU-	
SEQ ID NO: 103		G004-29 UAGCACCAUUUGAAGUCAGUGUU	Mutation
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	Insert.
SEQ ID NO: 120		G030-29 UAGCACCAUUUGAAAGUCAGUG--	
SEQ ID NO: 117		G027-29 UAGCACCAUUUGAAGGUCAGUGUU	Mut. + Insert.
SEQ ID NO: 116		G026-29 UAGCACCAUUUGAAGGUCAGUG--	
SEQ ID NO: 105		G006-29 UAGCACCAUUGAAGUCAGUGUU	Hybrid + Mut. +insert.
SEQ ID NO: 110		G020-29 UAGCACCAUUGAAGGUCAGUGUU	
SEQ ID NO: 109		G019-29 UAGCACCAUUGAAGGCAGUGUU	
SEQ ID NO: 100		G001-29 UAGCACCAUUGAAAGCAGUGUU	

FIG. 15

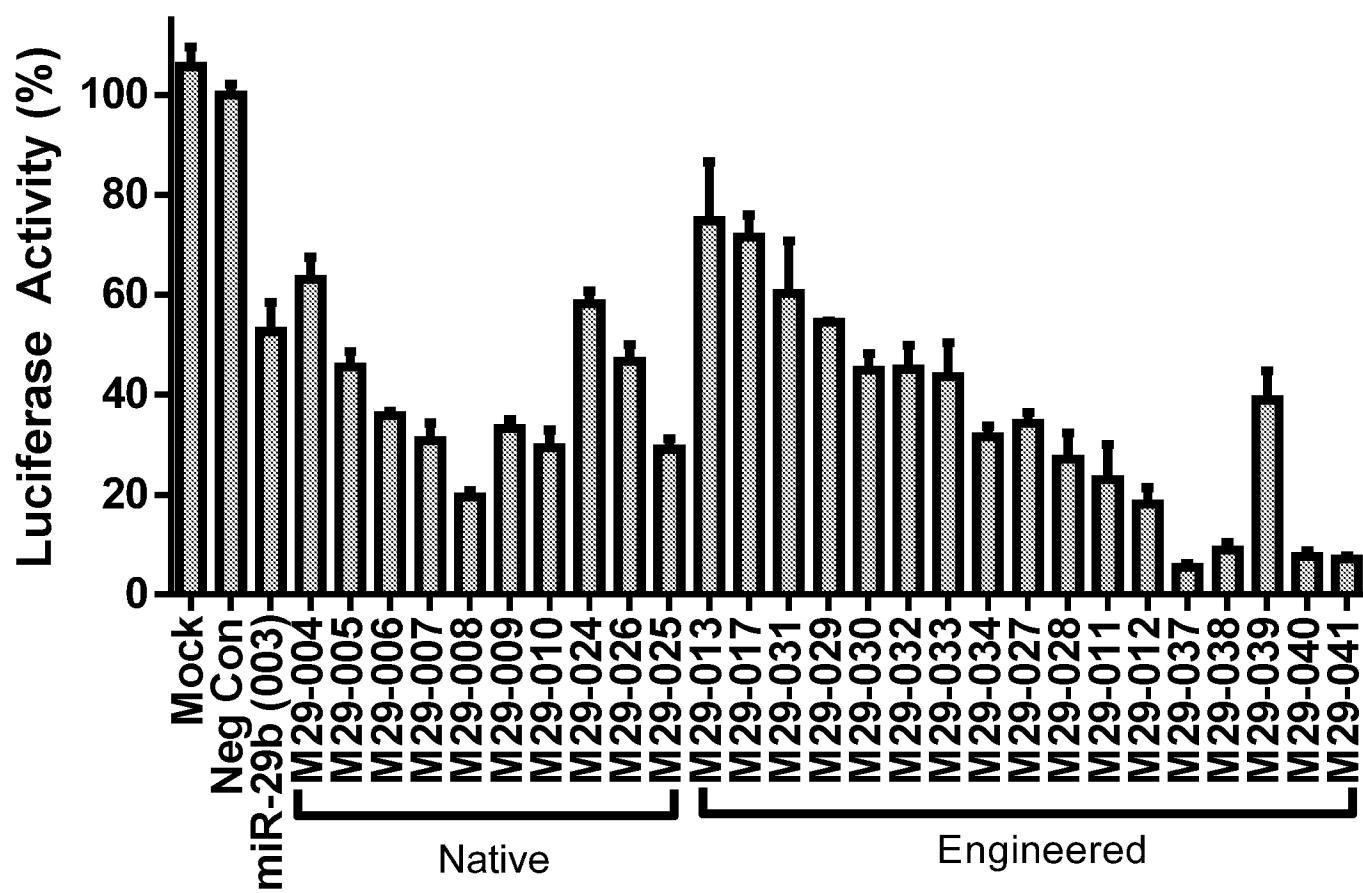


FIG. 17

miR-29b-1:

5'-GCUGGUUUCA AUGGUG UUAGA-3'

:|||:||||| ||||| :||

3'-UUGUGACUAAAGU UACCAC GAU-5'

U --

SEQ ID NO: 16

SEQ ID NO: 13

M29-004:

(Amino C6)-5'-GCUGGUUUCA AUGGUG UUA-3'

:|||:||||| ||||| :||

3'-UUGUGACUAAAGU UACCAC GAU-5'

U --

SEQ ID NO: 170

SEQ ID NO: 13

M29-012:

(Amino C6)-5'-CACUGAUUUCAGAU GGUGUUA-3'

||||| ||||| ||||| :||

3'-UUGUGACUAAAGUCUACCACGAU-5'

SEQ ID NO: 176

SEQ ID NO: 102

FIG. 18A

The figure is a gel electrophoresis image showing three rows of bands. The columns are labeled as follows: 'No serum', '0 min', '1 min', '5 min', '15 min', '30 min', '1 hr', '2 hr', and '4 hr'. The first three columns ('No serum', '0 min', '1 min') are grouped under the label '+ Human serum'. The rows are labeled on the left as 'miR-29b-1', 'M29-004', and 'M29-012'. For 'miR-29b-1' and 'M29-004', there is a single prominent band at the '0 min' time point, which disappears by '1 min' and remains absent through '4 hr'. For 'M29-012', there is a prominent band at '0 min' and a series of bands of decreasing intensity at '1 min', '5 min', '15 min', and '30 min', with the band being nearly absent at '1 hr' and '2 hr'.

FIG. 18B

M29-024:

(Amino C6)-5'-ACUGAUUUCAGAU^{GU}GGUGUUA-3'

|||||:|||||:

3'-UuGuGaCuAaAgUuUaCcAcGaU-5'

SEQ ID NO:173

SEQ ID NO:127

M29-026:

(Amino C6)-5'-GCUGGUUUCAGAU^{GU}GGUGUUA-3'

:|||:|||||:|||||:|

3'-UuGuGaCuAaAgUuUaCcAcGaU-5'

SEQ ID NO:171

SEQ ID NO:127

M29-028:

(Amino C6)-5'-CACUGAUUUCAGAU^{GU}GGUGUUA-3'

|||||:|||||:|||||:

3'-UuGuGaCuAaAgUcUaCcAcGaU-5'

SEQ ID NO:176

SEQ ID NO:128

FIG. 19A

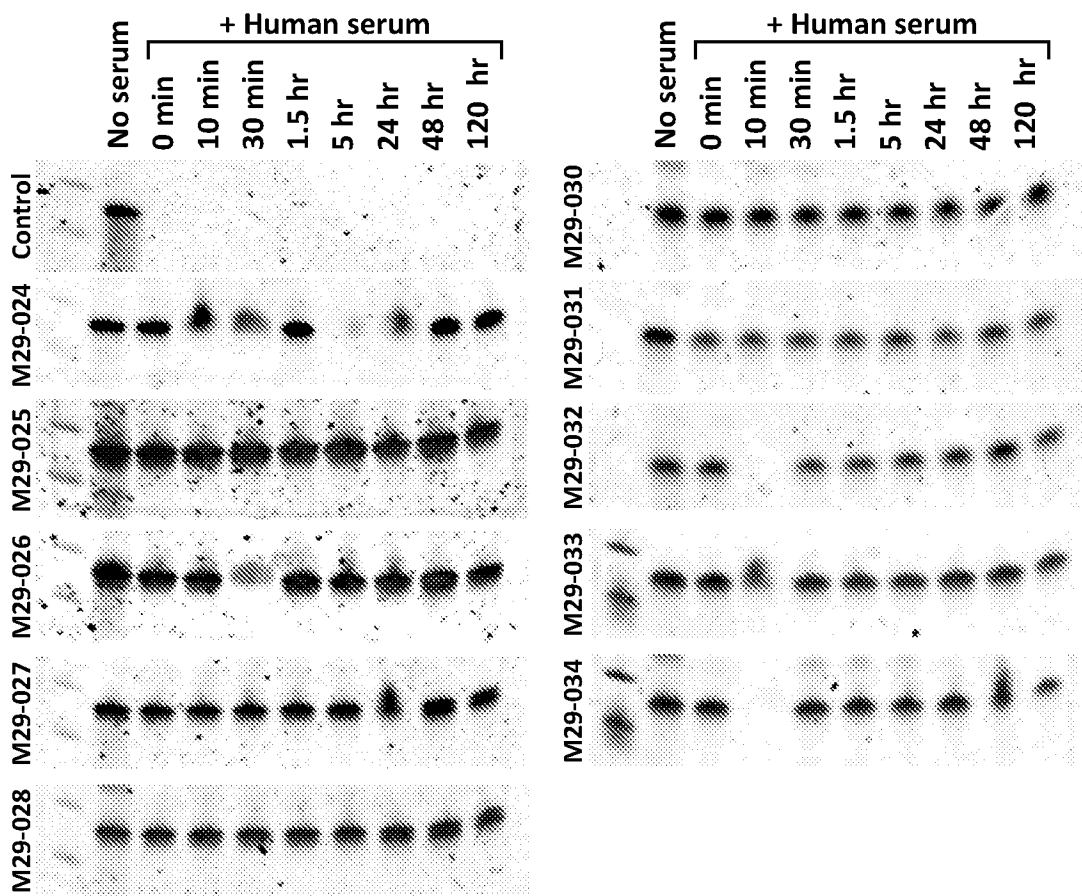


FIG. 19B

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

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

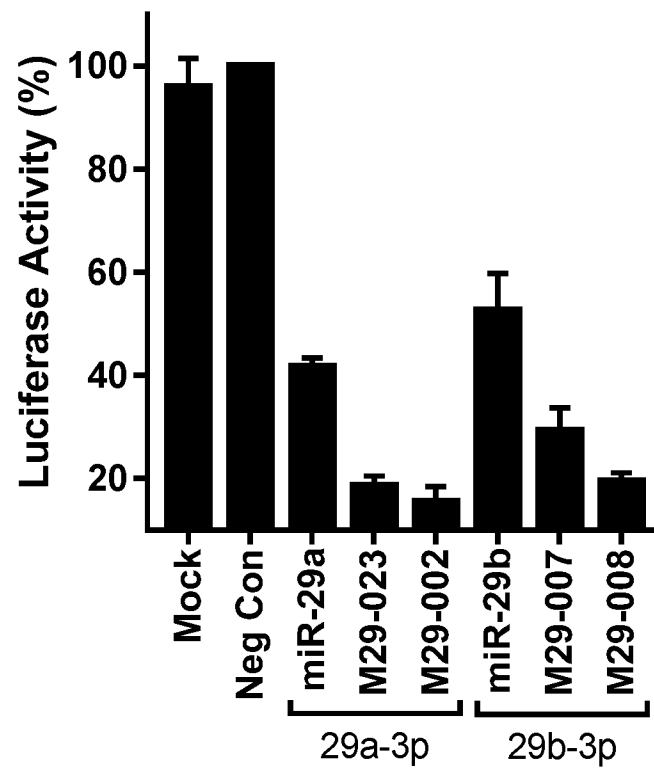
FIG. 20A

miR-29b-1
 5' - GCUGGUUUC U GU 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' - ACUGAUUUCAGAUUGGUGUUA-3' P007-29 SEQ ID NO: 173
 M29-007 ||||| ||||:||
 3' -UUGUGACUAAAGUUUACCACGAU-5' miR-29b-3p SEQ ID NO: 13

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

FIG. 20B

**FIG. 20C**

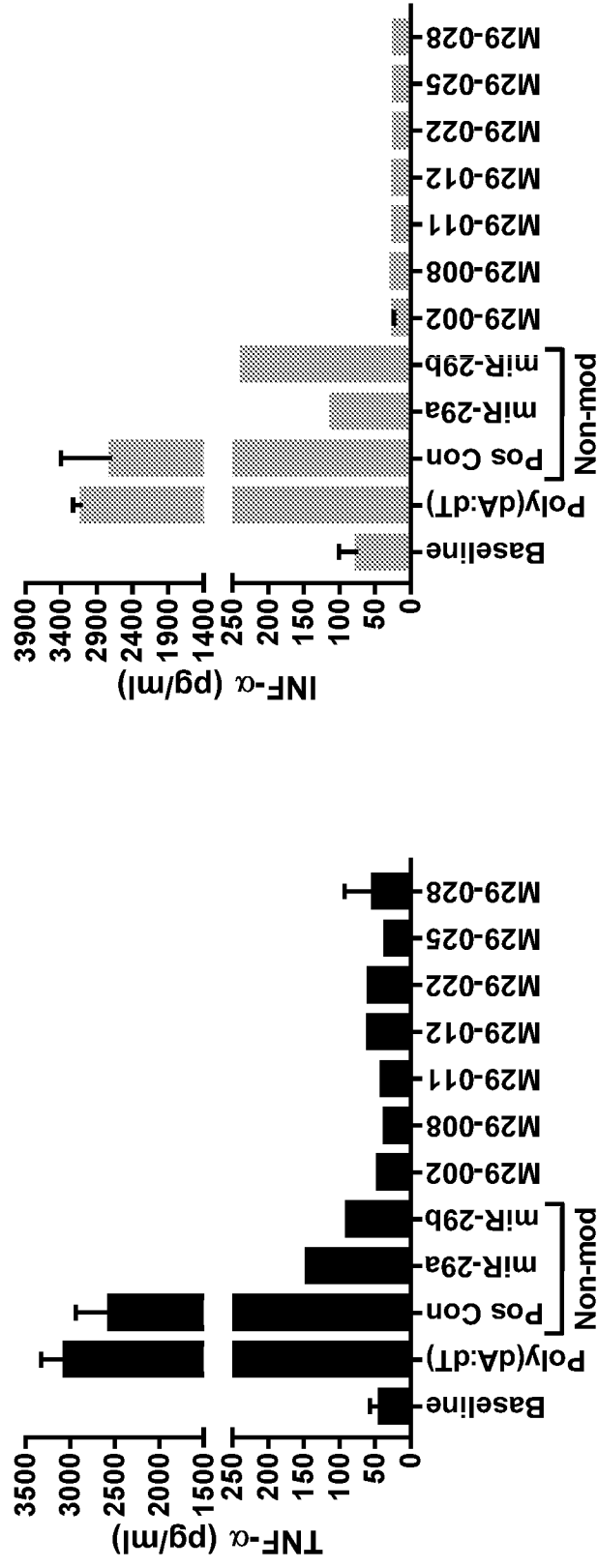


FIG. 21

<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				

<div>UC CC</div>			
HIV-1 NEF site:	5' -	CACUGA UUUGGAUGGUGCUA -3'	SEQ ID NO: 470
		::	
G003-29:	3' -	GUGACU -AAGUCUACACGAU -5'	SEQ ID NO: 102
		UU A	
<div>ΔG = -32.6 kcal/mol</div>			
<div>UC A</div>			
HIV-1 NEF site:	5' -	CACUG CCUUUGGAUGGUGCUA -3'	SEQ ID NO: 470
		:::	
G031-29:	3' -	GUGAC-GGAAGUUUACACGAU -5'	SEQ ID NO: 121
		UU	
<div>ΔG = -35.7 kcal/mol</div>			
<div>UC</div>			
HIV-1 NEF site:	5' -	CACUGACCUUUGGAUGGUGCUA -3'	SEQ ID NO: 470
		:::	
G020-29:	3' -	GUGACUGGAAGUUUACACGAU -5'	SEQ ID NO: 110
		UU	
<div>ΔG = -43.4 kcal/mol</div>			

FIG. 22B

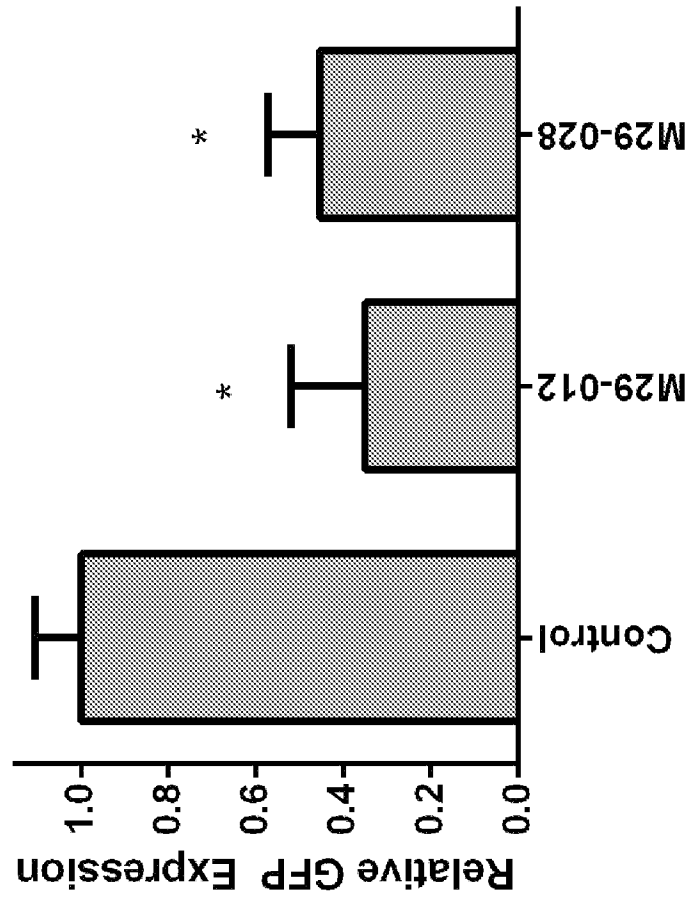


FIG. 22C

FIG. 23A

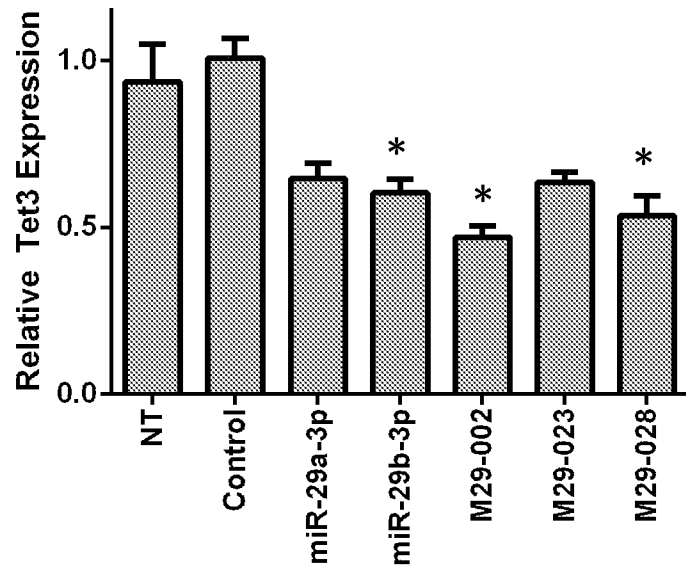


FIG. 23B

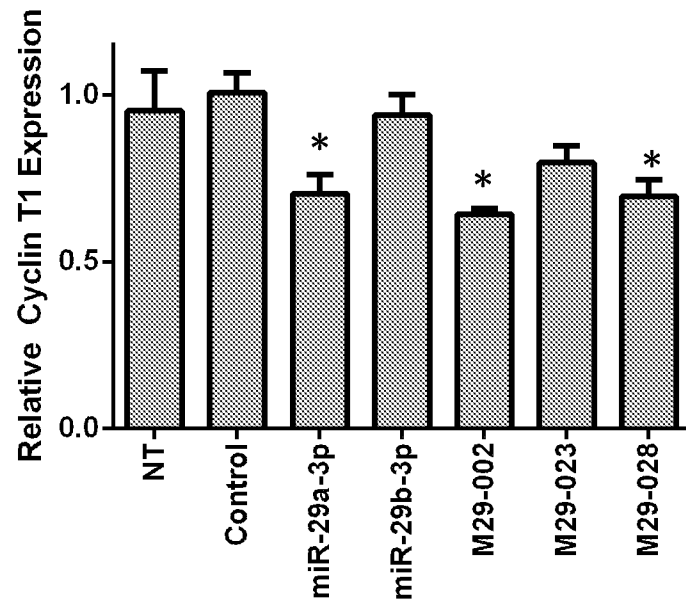
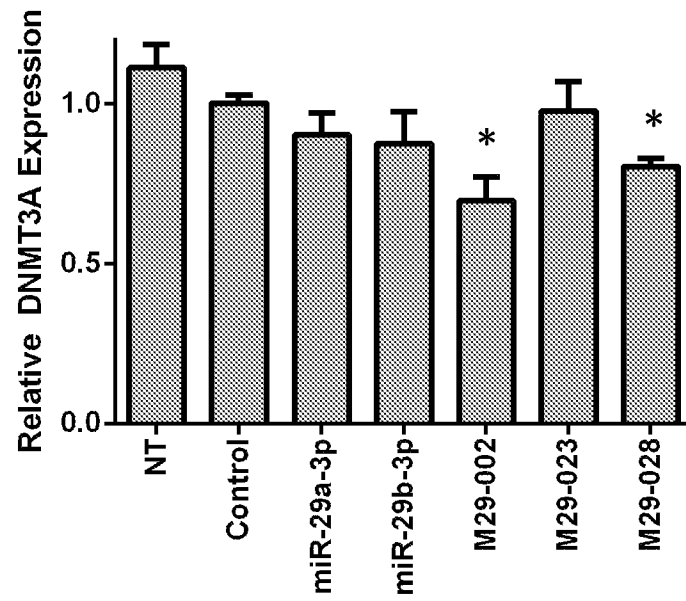


FIG. 23C



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

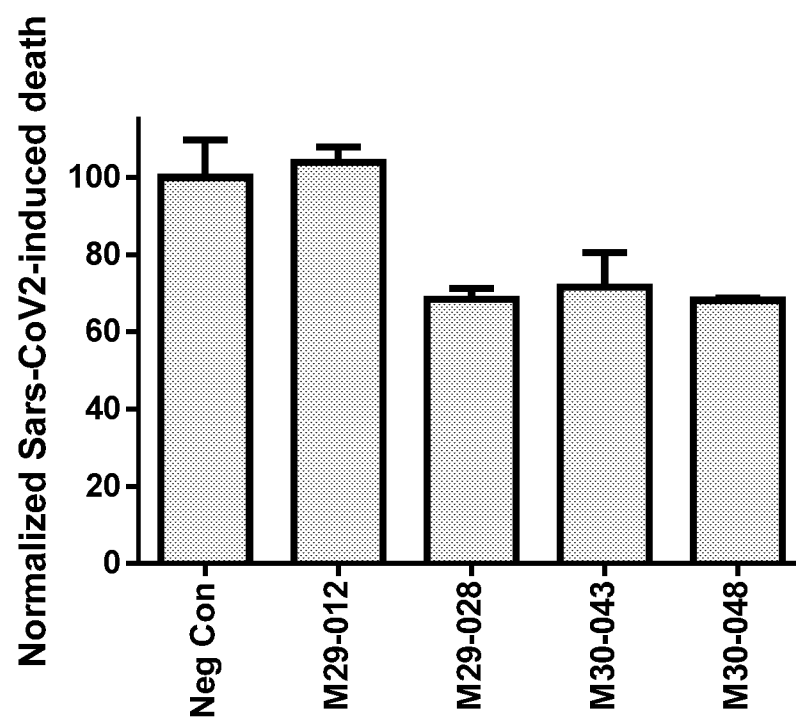


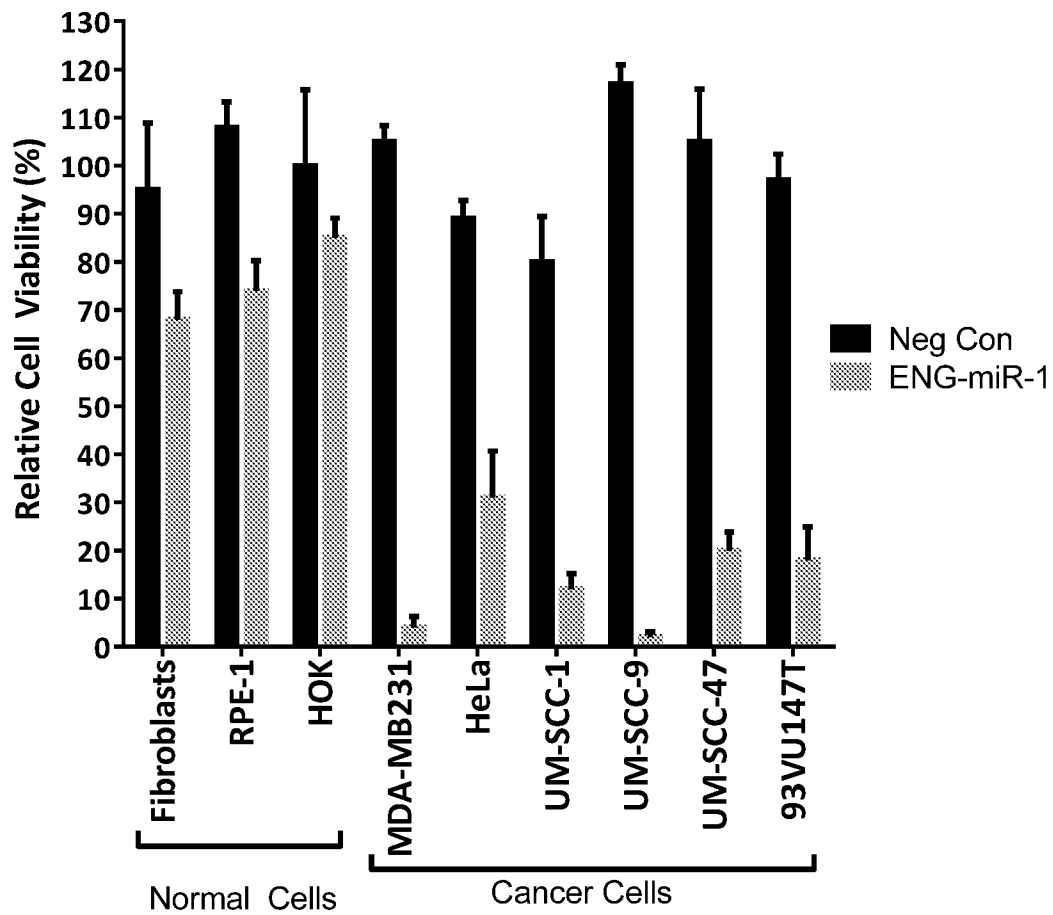
FIG. 25C

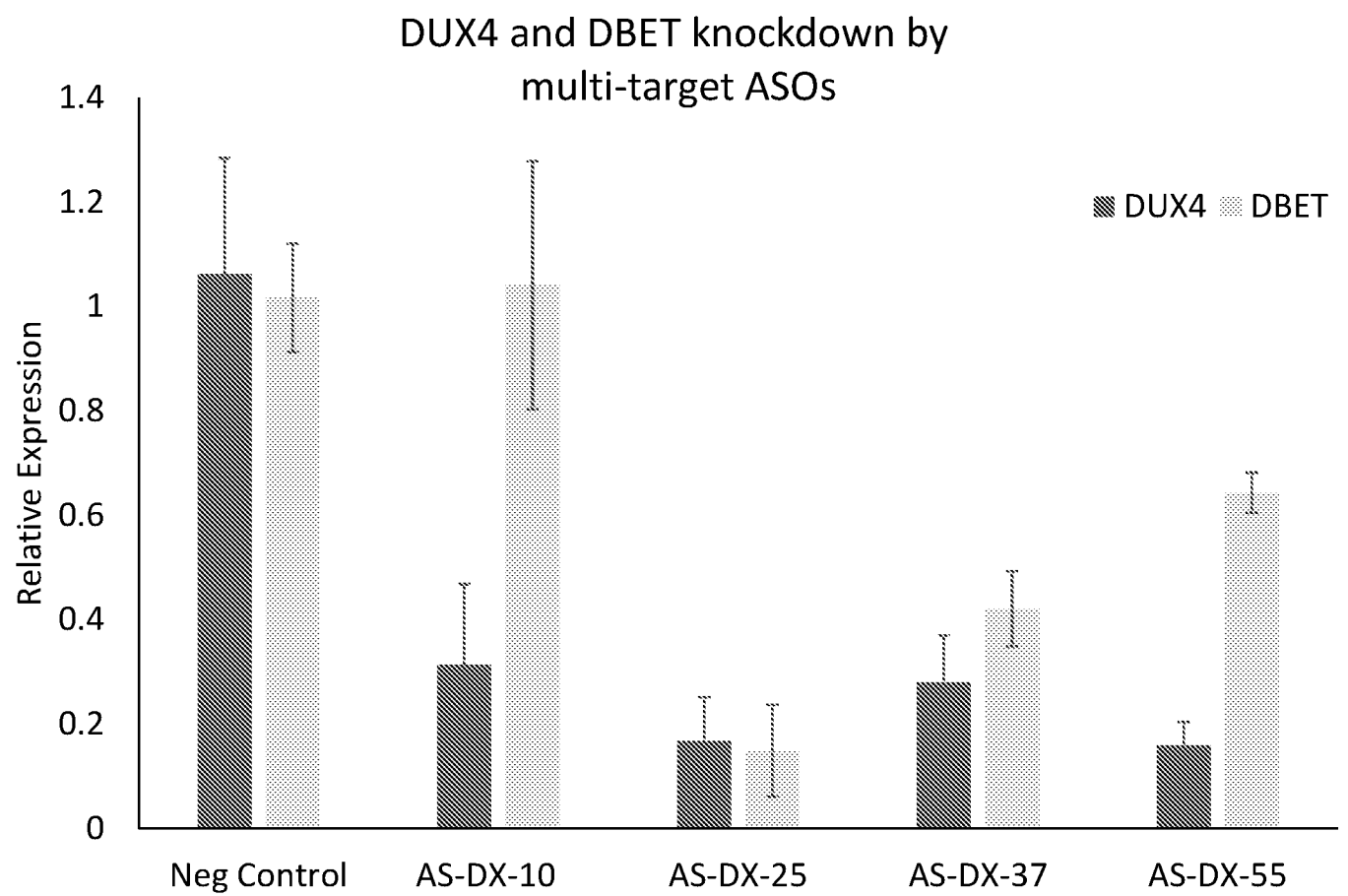
Calculated Free Energy Requirements for Target Recognition of Mimic Guide Strands to HCV Genotype 1 Transcript

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**

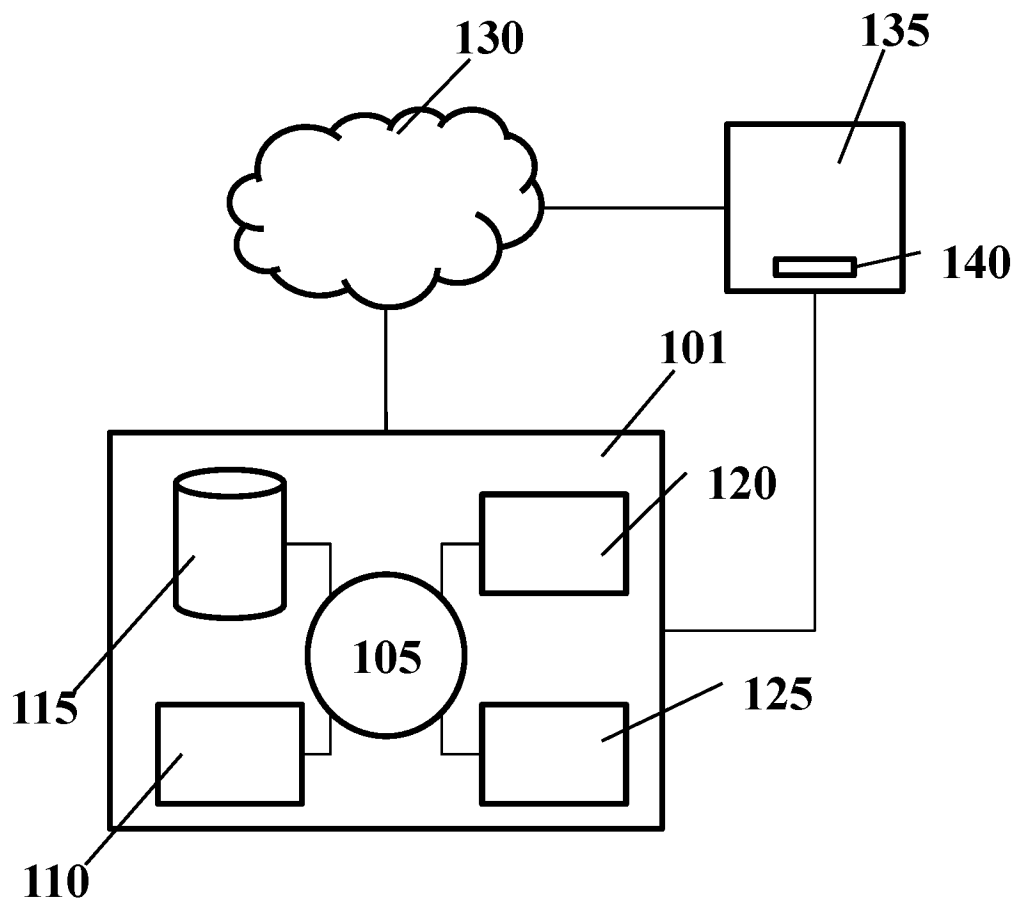
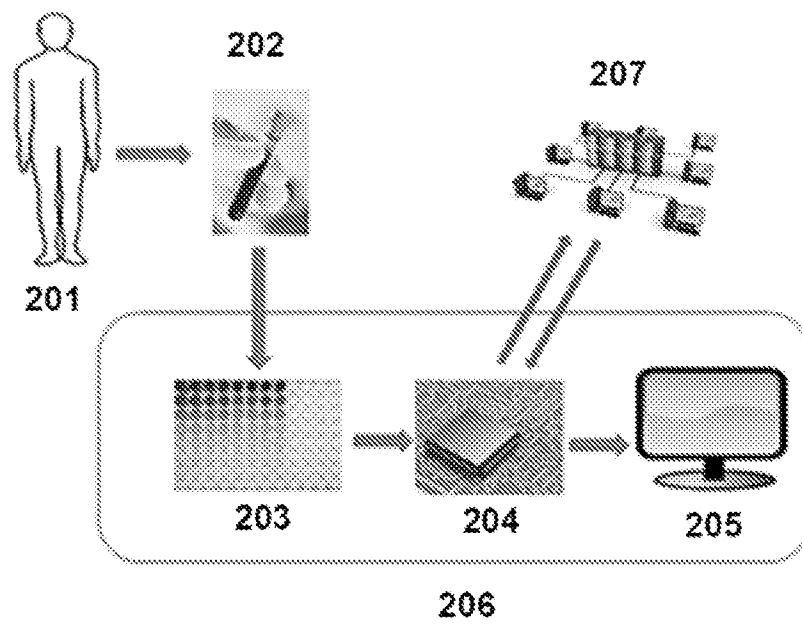


FIG. 29

**FIG. 30**