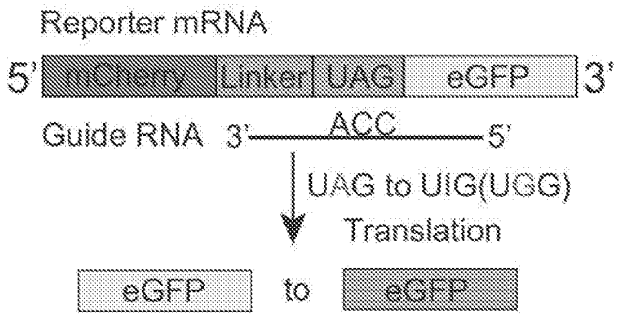


Figure 1A

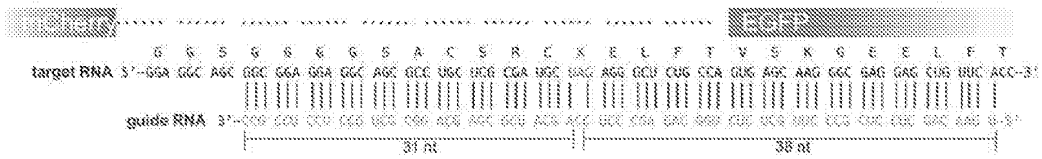


Figure 1B

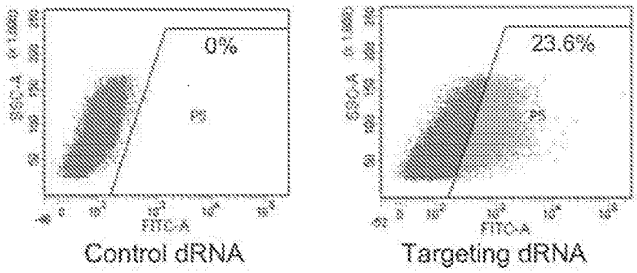


Figure 1C

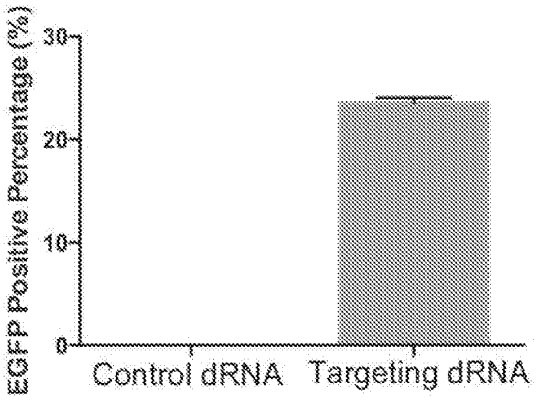


Figure 1D

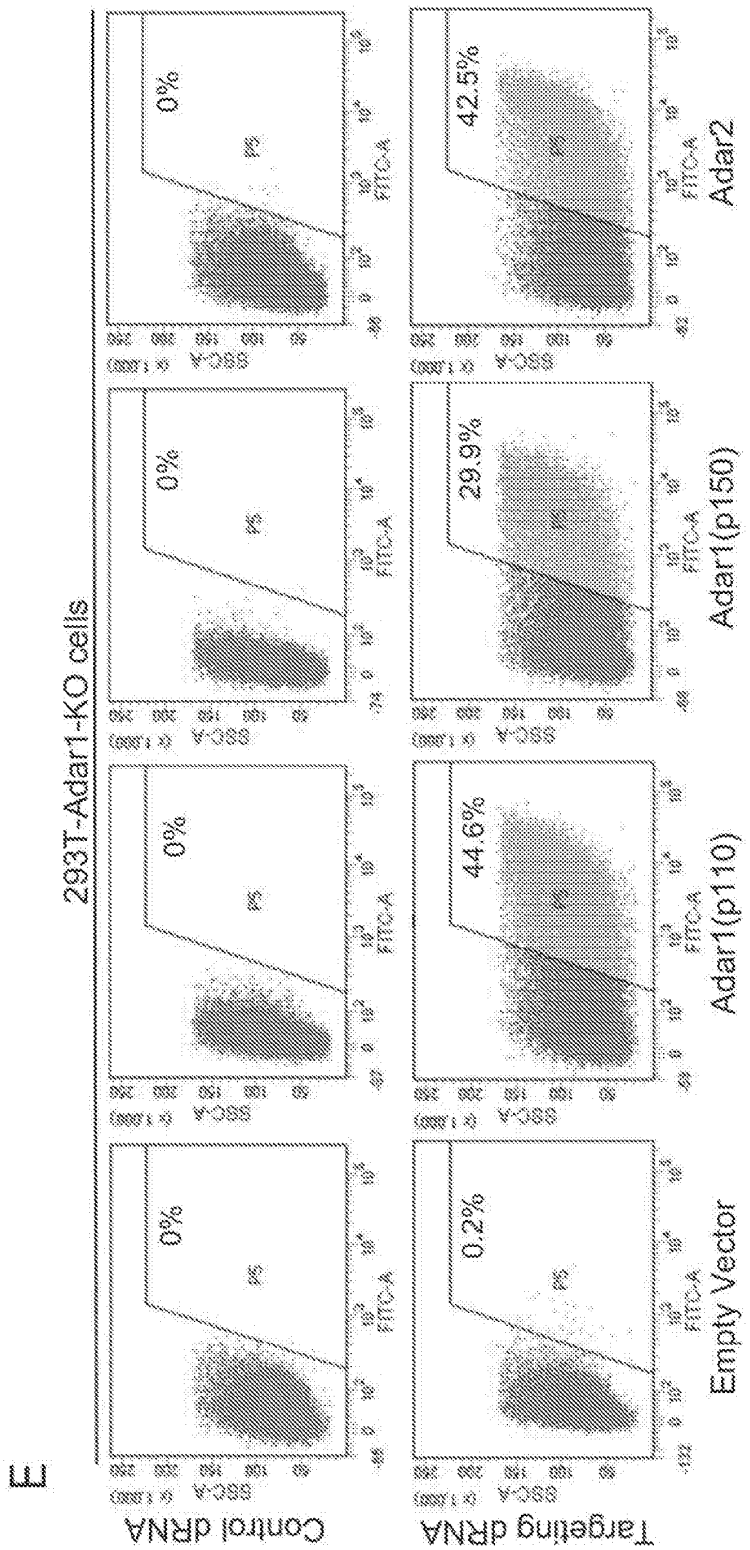

E
293T-Adar1-KO cells
Control dRNA
Targeting dRNA
Empty Vector
Adar1(p110)
Adar1(p150)
Adar2
0%
0.2%
44.6%
29.9%
42.5%
P5
SSC-A
FITC-A

Figure 1E

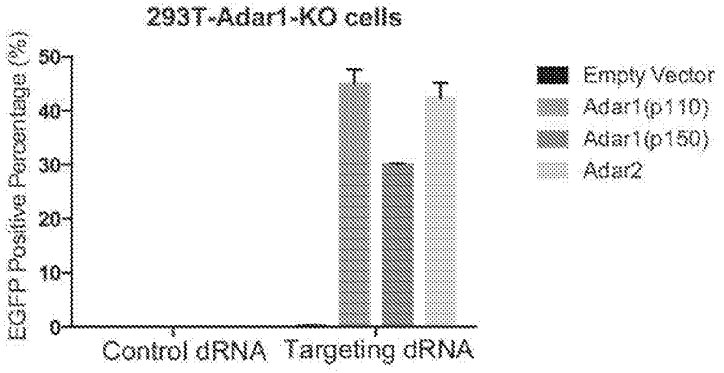


Figure 1F

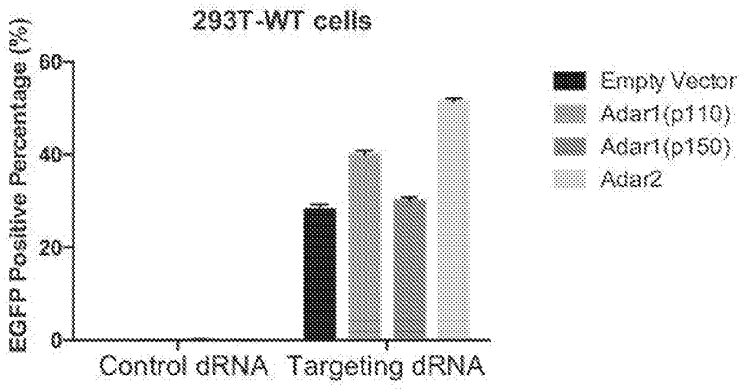


Figure 1G

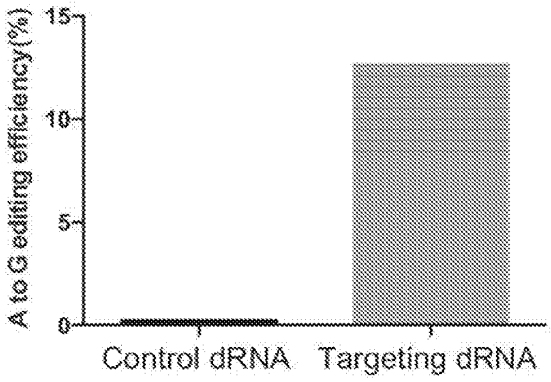


Figure 1H

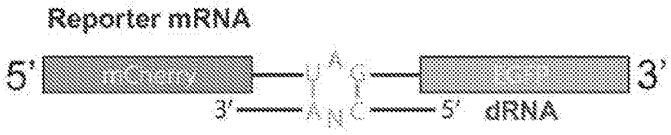


Figure 2A

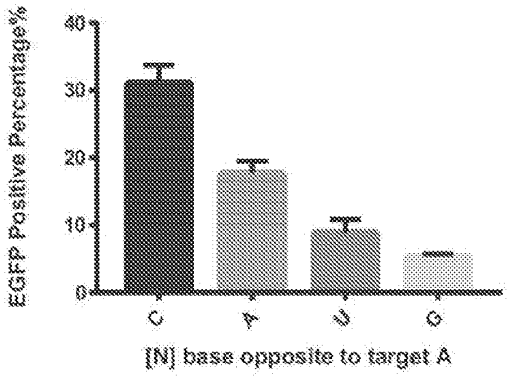


Figure 2B



Figure 2C

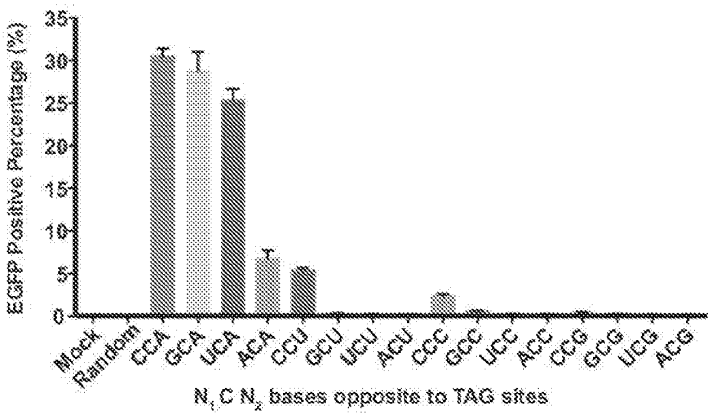


Figure 2D

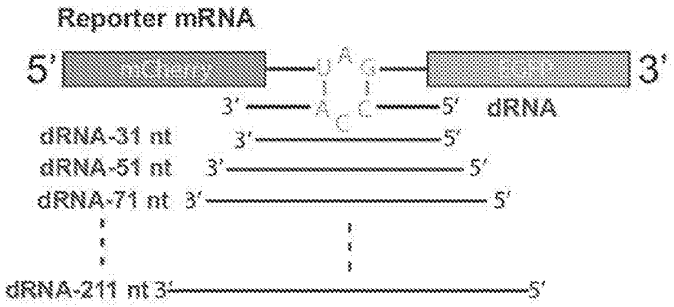


Figure 2E

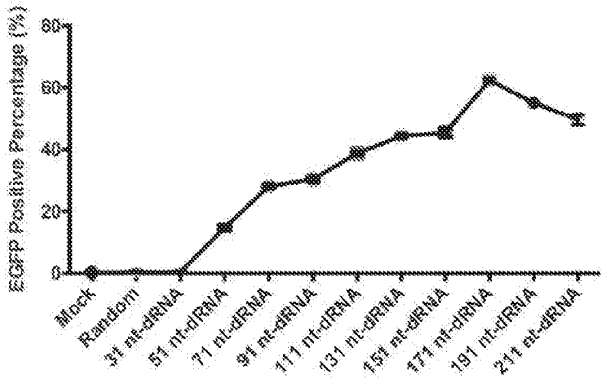


Figure 2F

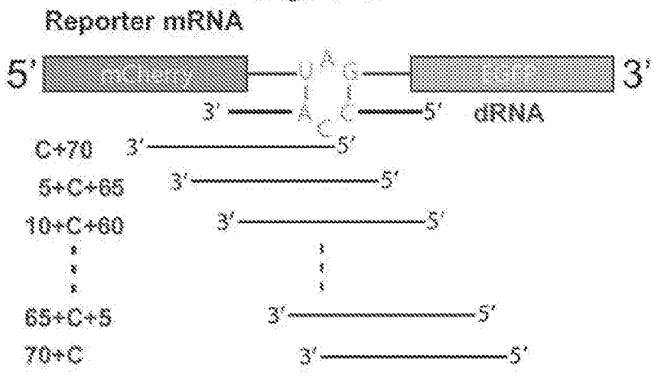


Figure 2G

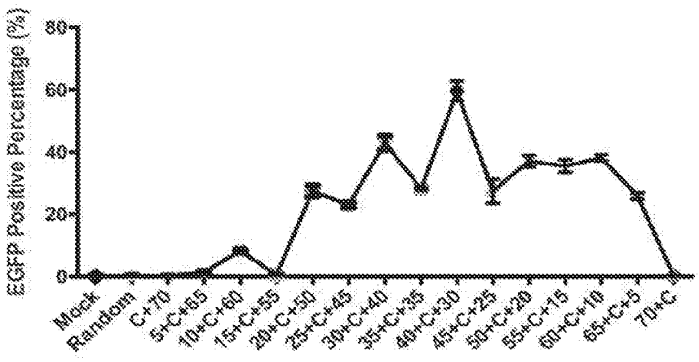


Figure 2H

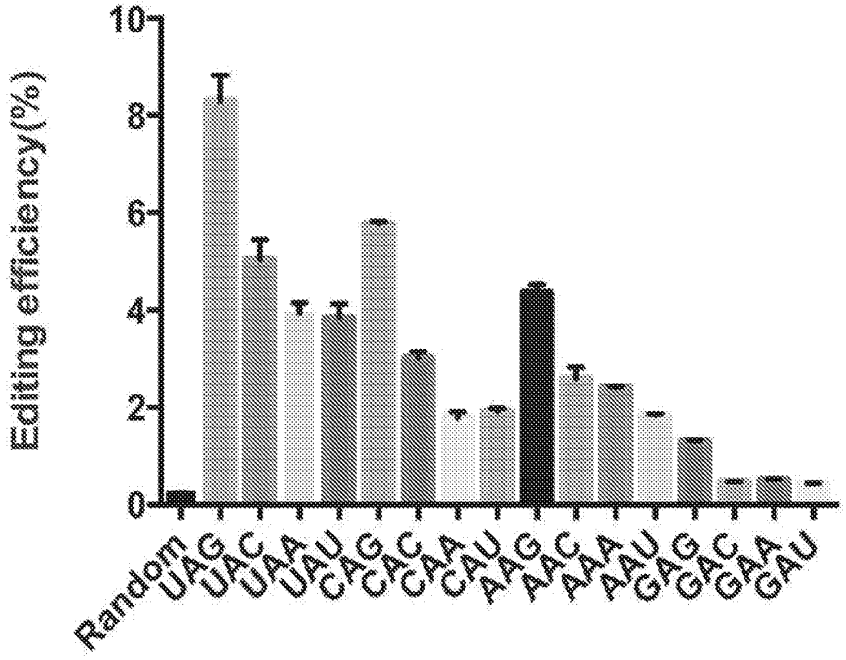


Figure 3A

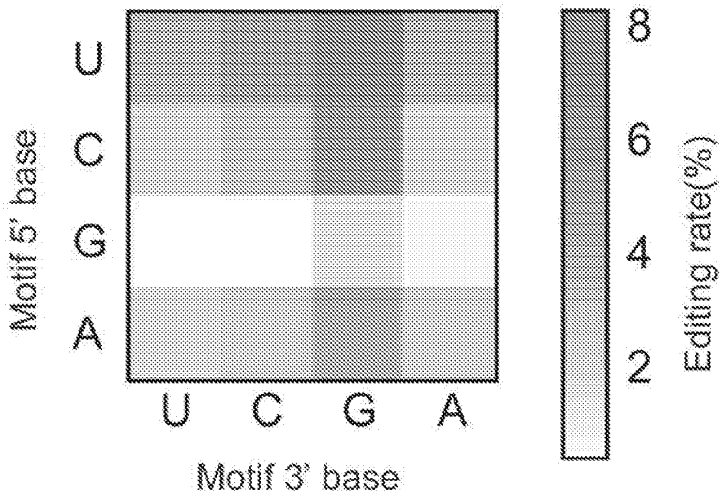


Figure 3B

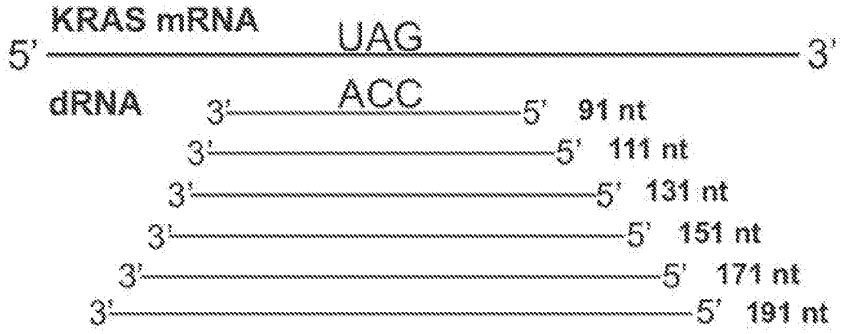


Figure 4A

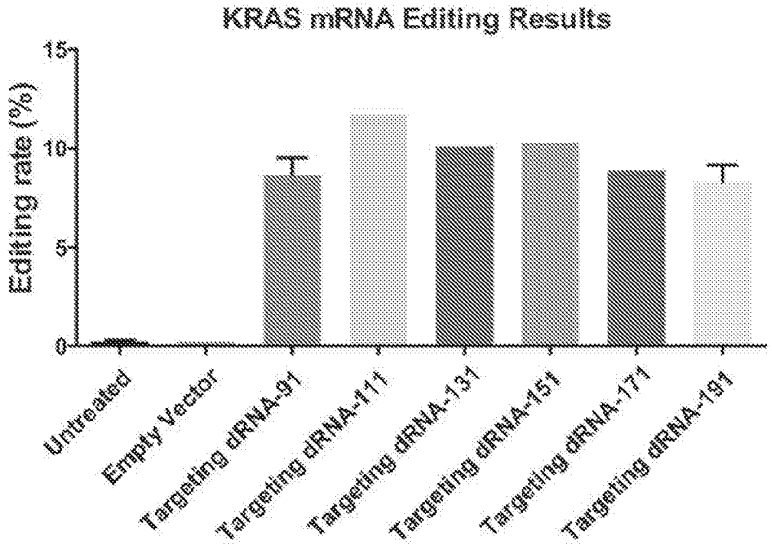


Figure 4B

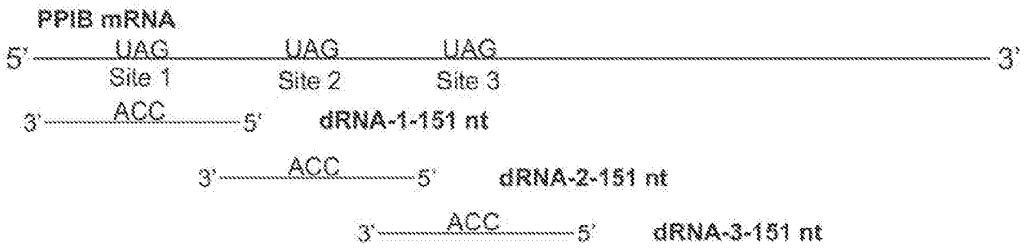


Figure 4C

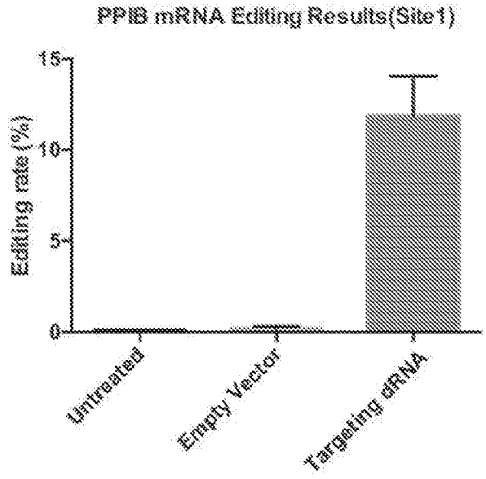


Figure 4D

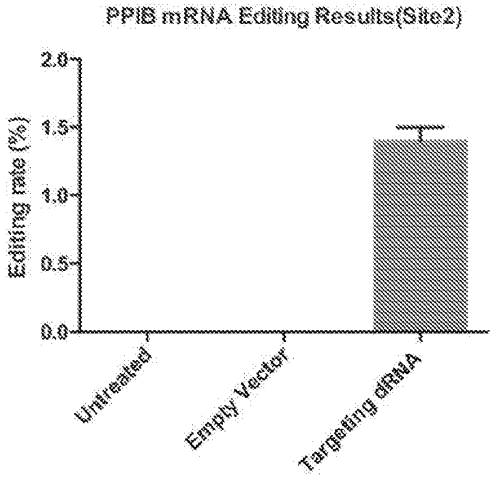


Figure 4E

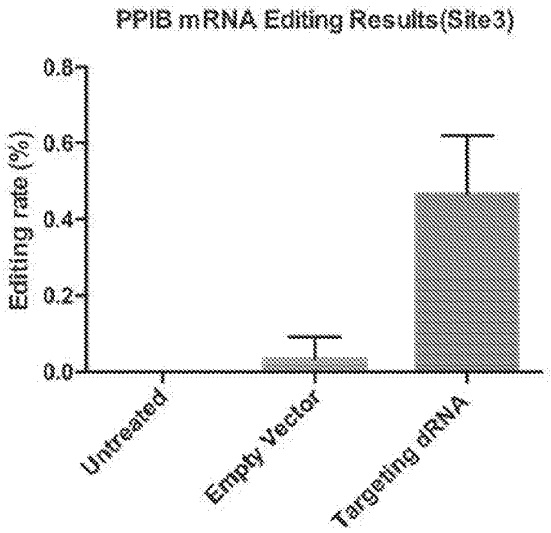


Figure 4F

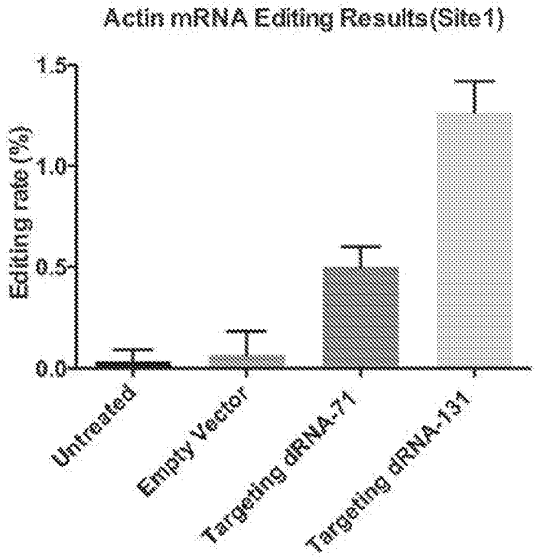


Figure 4H

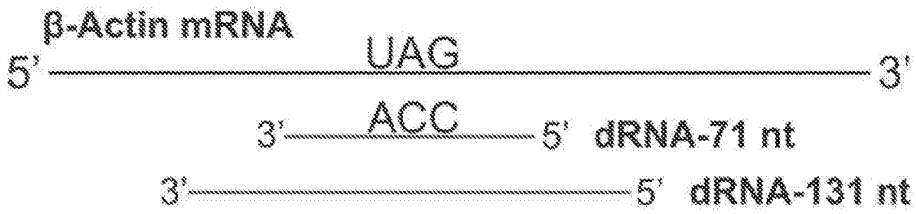


Figure 4G

Figure 5A

Figure 5B

Figure 5C

Figure 5D

A-G mismatch sites

dRNA-AG1: A_{41} , A_{46} , A_{74}

dRNA-AG2: A_{41} , A_{43} , A_{45} , A_{46} , A_{74} , A_{79}

dRNA-AG3: A_{31} , A_{32} , A_{33} , A_{41} , A_{43} , A_{45} , A_{46} , A_{47} , A_{74} , A_{79}

dRNA-AG4: A_{7} , A_{31} , A_{32} , A_{33} , A_{40} , A_{41} , A_{43} , A_{45} , A_{46} , A_{47} , A_{74} , A_{79} , A_{95}

Figure 5E

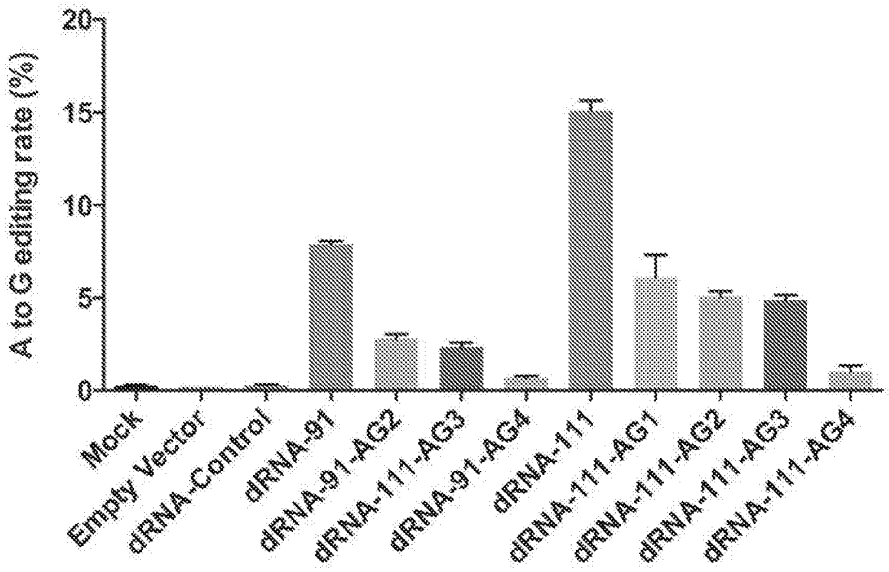


Figure 5F

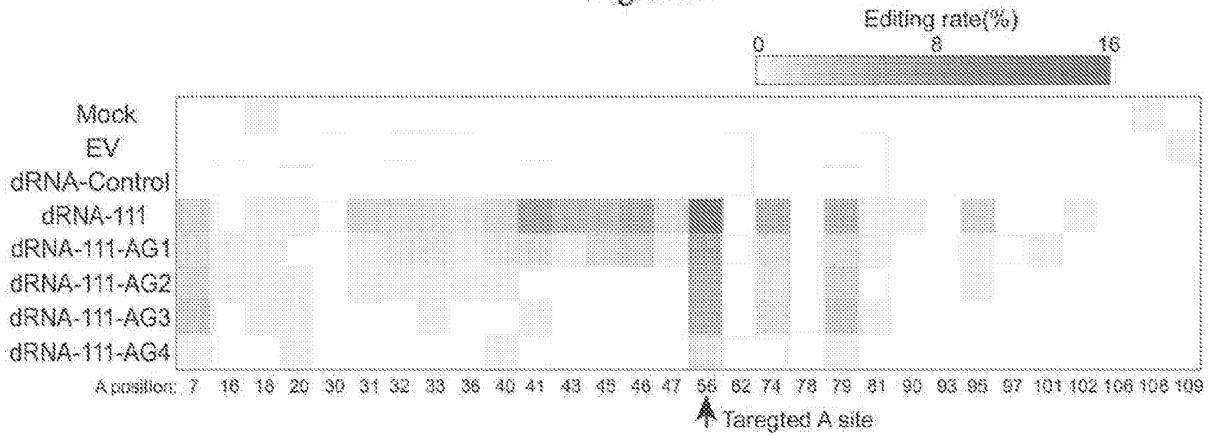


Figure 5G

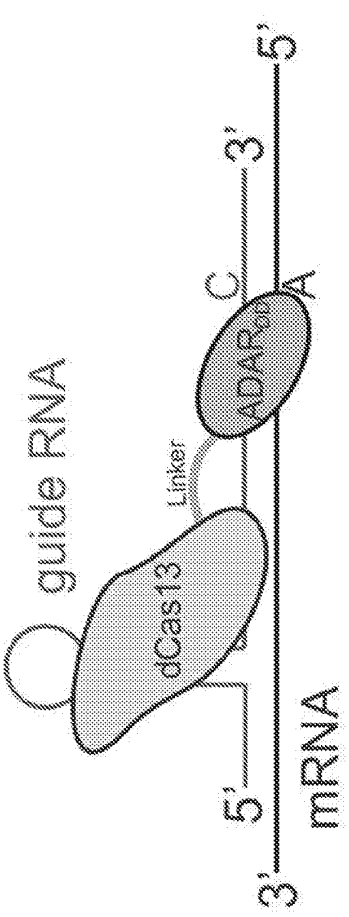

guide RNA
dCas13
Linker
ADAR
C
A
3'
5'
5'
3'
mRNA

FIG.6A

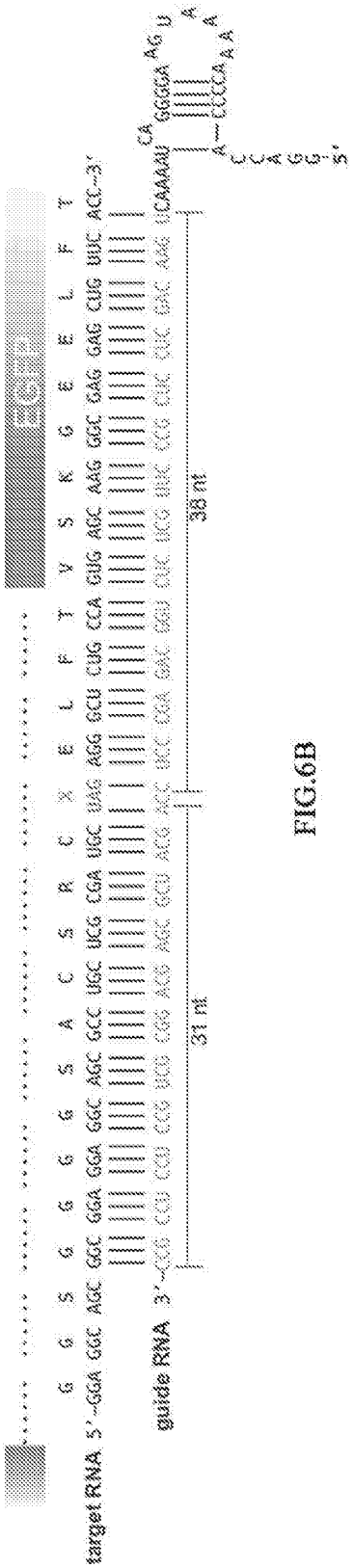

target RNA
guide RNA
31 nt
38 nt
ACC–3'

FIG.6B

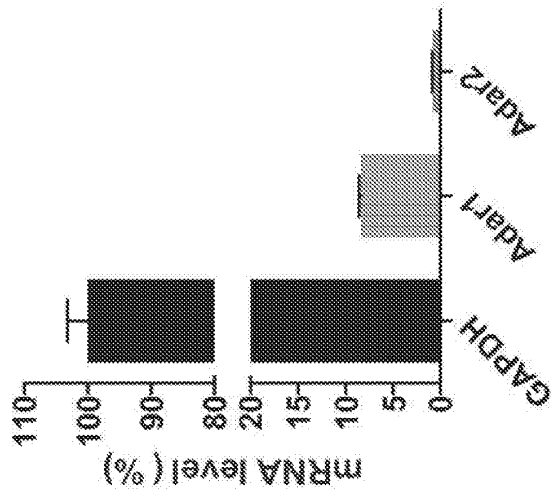

mRNA level (%)
110
100
90
80
20
15
10
5
0
GAPDH
Adar1
Adar2

FIG.6D

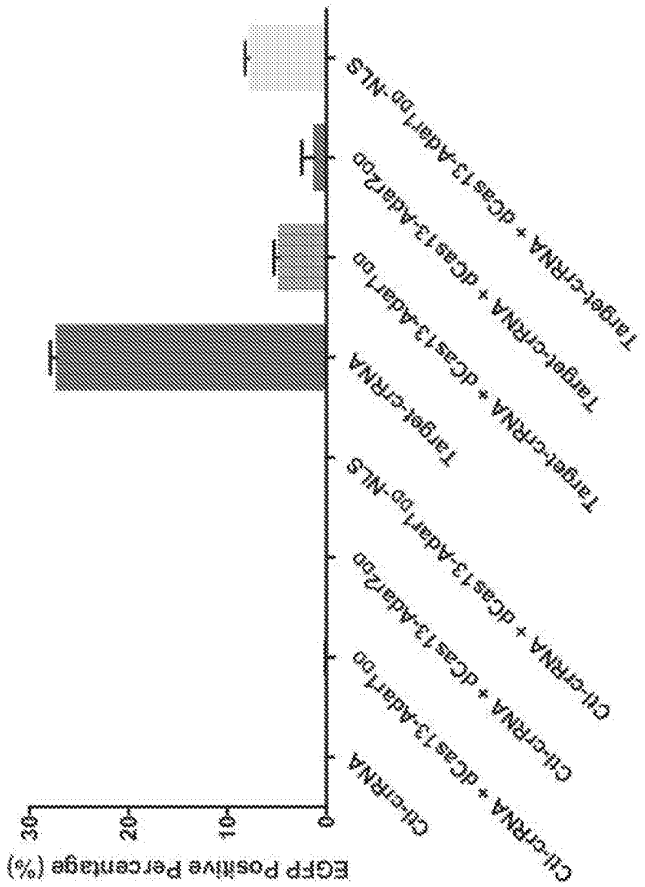

EGFP Positive Percentage (%)
30
20
10
0
Cli-crRNA
Cli-crRNA + dCas13-Adar1DD
Cli-crRNA + dCas13-Adar2DD
Cli-crRNA + dCas13-Adar1DD-NLS
Target-crRNA
Target-crRNA + dCas13-Adar1DD
Target-crRNA + dCas13-Adar2DD
Target-crRNA + dCas13-Adar1DD-NLS

FIG.6C

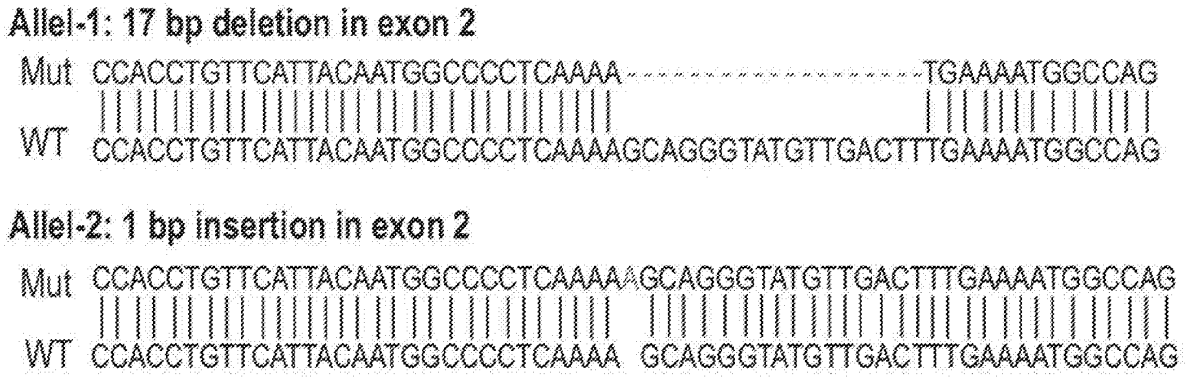

Allel-1: 17 bp deletion in exon 2
Mut CCACCTGTTCATTACAATGGCCCCTCAAAA----------TGAAAATGGCCAG
WT CCACCTGTTCATTACAATGGCCCCTCAAAAGCAGGGTATGTTGACTTTGAAAATGGCCAG
Allel-2: 1 bp insertion in exon 2
Mut CCACCTGTTCATTACAATGGCCCCTCAAAAAGCAGGGTATGTTGACTTTGAAAATGGCCAG
WT CCACCTGTTCATTACAATGGCCCCTCAAAA GCAGGGTATGTTGACTTTGAAAATGGCCAG

FIG.6E

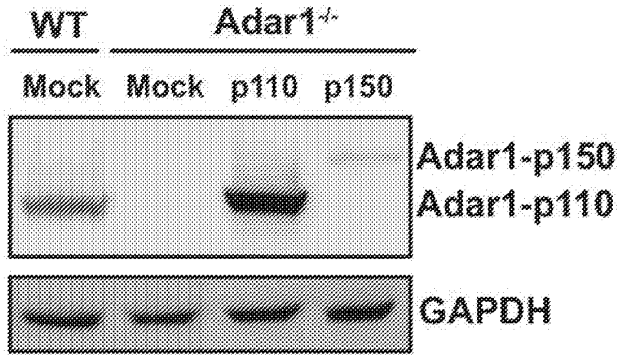

WT
Adar1-/-
Mock
Mock
p110
p150
Adar1-p150
Adar1-p110
GAPDH

FIG.6F

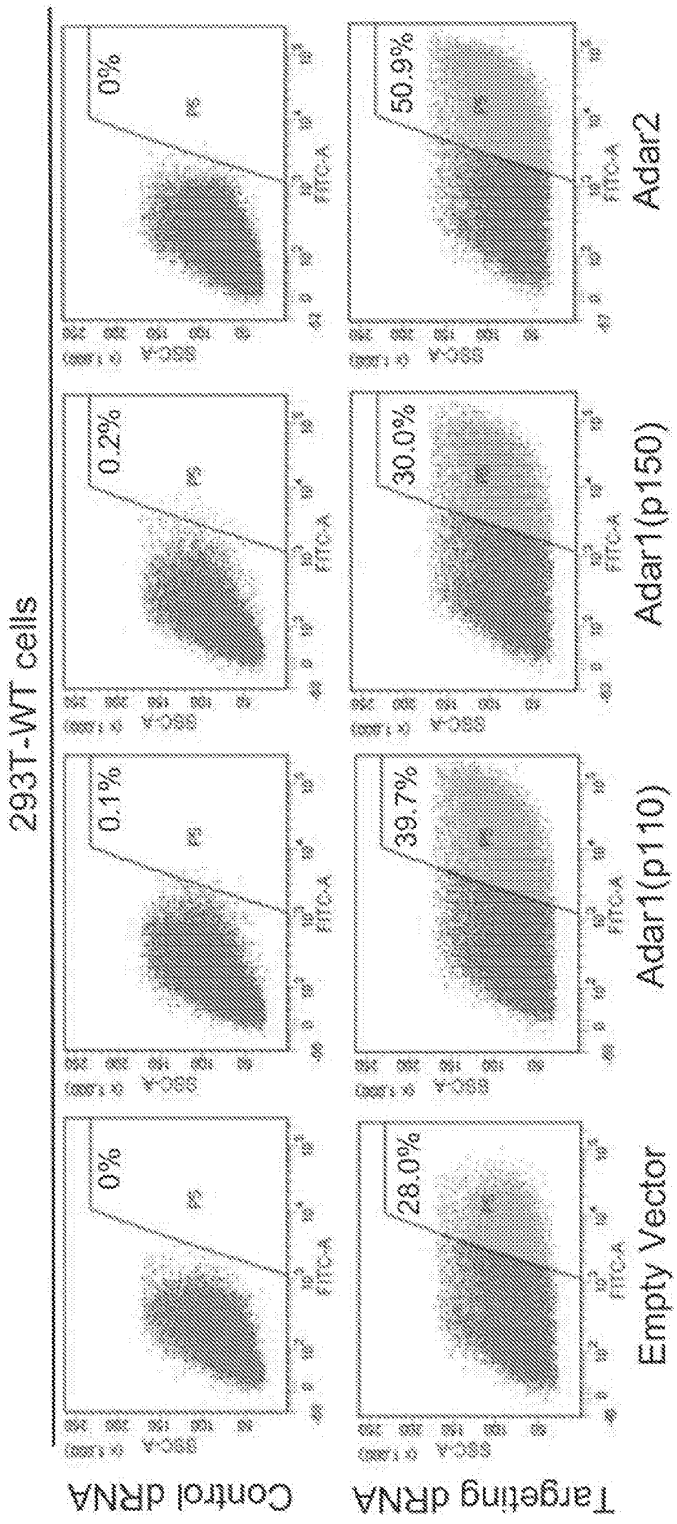

293T-WT cells
Control dRNA
Targeting dRNA
Empty Vector
Adar1(p110)
Adar1(p150)
Adar2
0%
0.1%
0.2%
0%
28.0%
39.7%
30.0%
50.9%
FITC-A
SSC-A

FIG.6G

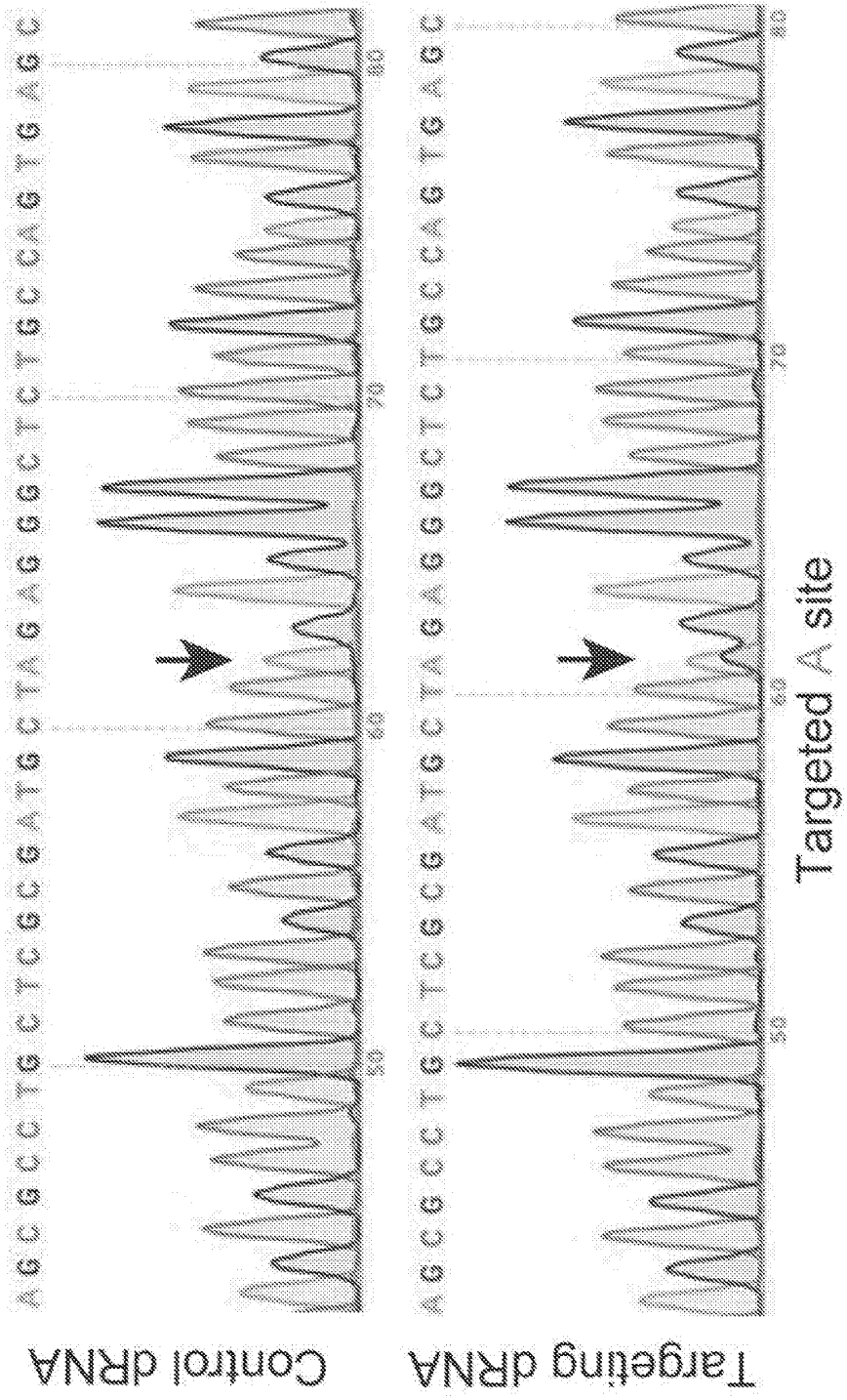

Control dRNA
Targeting dRNA
A G C G C C T G C T C C G C A T G C T A G A G G G C T C T G C C A G T G A G C
50
60
70
80
Targeted A site

FIG.6H

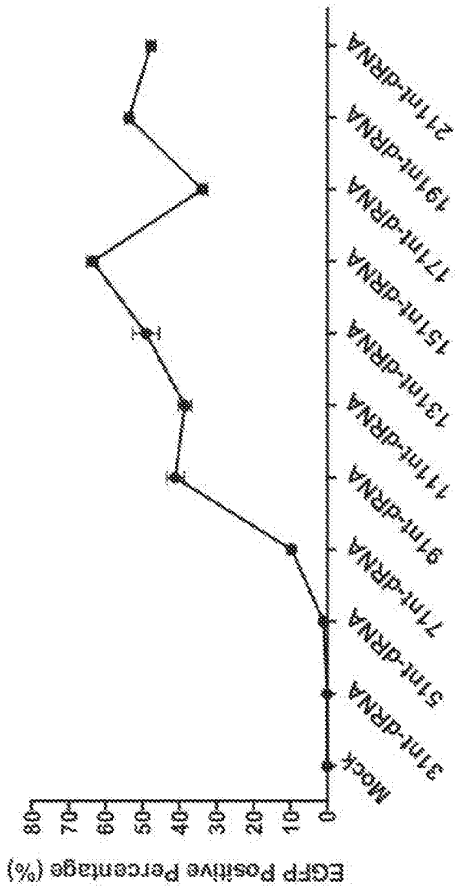
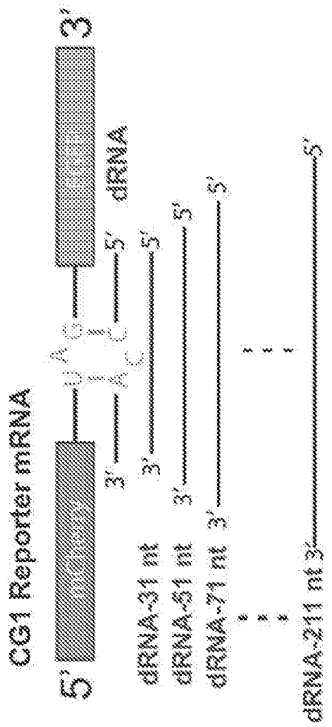
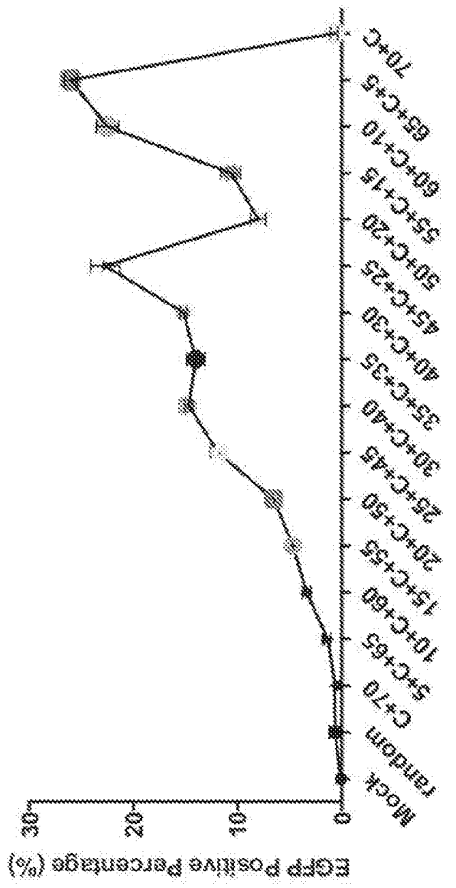

EGFP Positive Percentage (%)
0
10
20
30
40
50
60
70
80
Mock
3'nt-dRNA
5'nt-dRNA
7'nt-dRNA
9'nt-dRNA
11'nt-dRNA
13'nt-dRNA
15'nt-dRNA
17'nt-dRNA
19'nt-dRNA
21'nt-dRNA

FIG.7A


CG1 Reporter mRNA
5'
3'
dRNA
dRNA-31 nt
dRNA-51 nt
dRNA-71 nt
dRNA-211 nt


EGFP Positive Percentage (%)
30
20
10
0
Mock
random
C+70
5+C+65
10+C+60
15+C+55
20+C+50
25+C+45
30+C+40
35+C+35
40+C+30
45+C+25
50+C+20
55+C+15
60+C+10
65+C+5
70+C

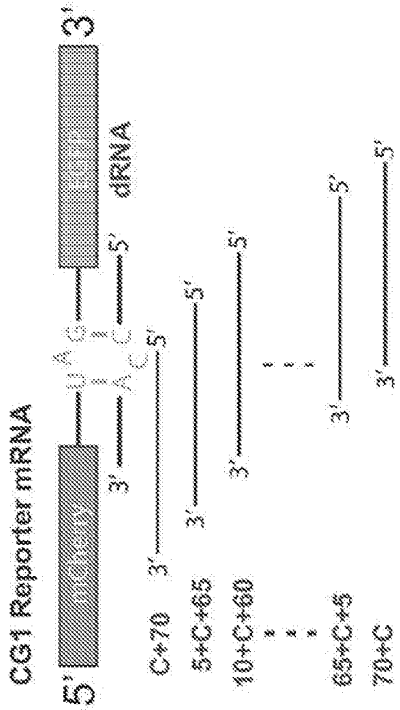

CG1 Reporter mRNA
5'
3'
AUG
3'
5'
dRNA
C+70
5+C+65
10+C+60
65+C+5
70+C

FIG.7B

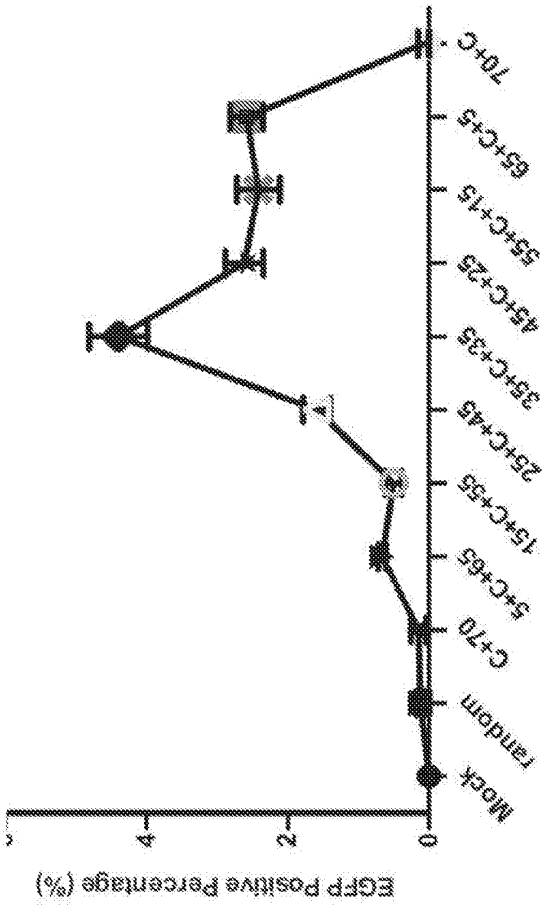
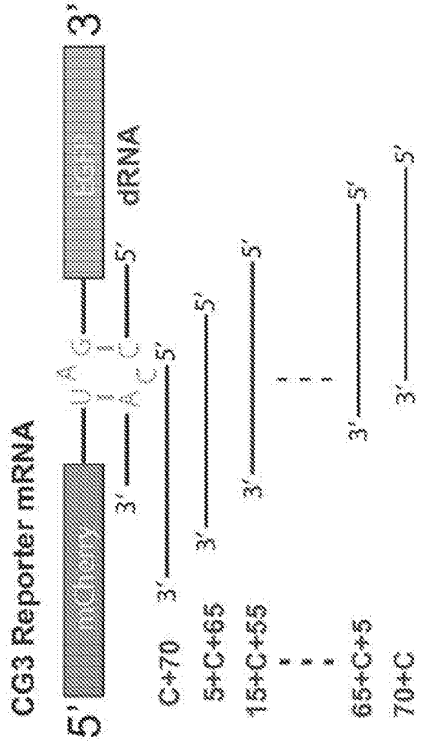

EGFP Positive Percentage (%)
0
2
4
Mock
random
C+70
5+C+65
15+C+55
25+C+45
35+C+35
45+C+25
55+C+15
65+C+5
70+C

FIG.7C


CG3 Reporter mRNA
5'
3'
dRNA
C+70
5+C+65
15+C+55
65+C+5
70+C

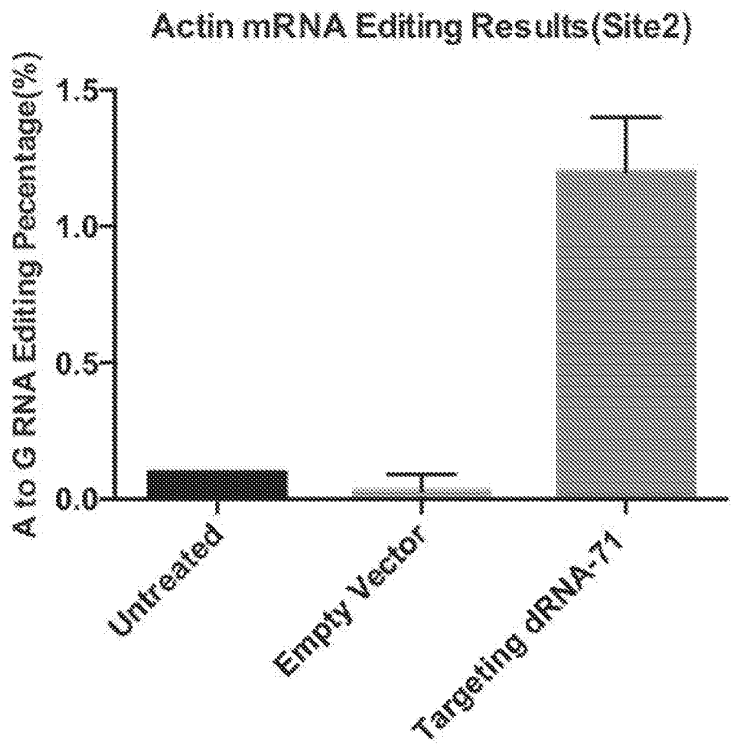

Actin mRNA Editing Results(Site2)
A to G RNA Editing Pecentage(%)
1.5
1.0
0.5
0.0
Untreated
Empty Vector
Targeting dRNA-71

FIG.8A

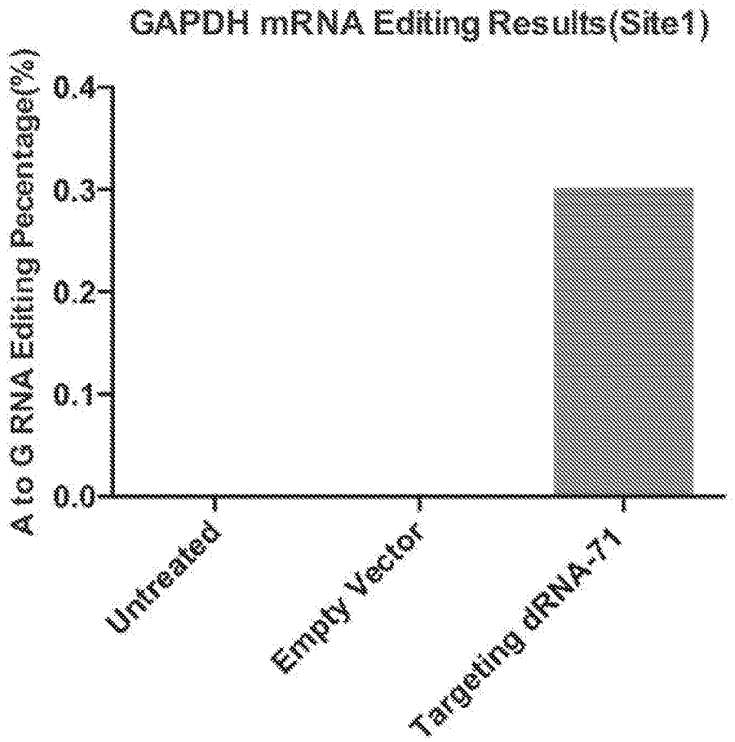

GAPDH mRNA Editing Results(Site1)
A to G RNA Editing Pecentage(%)
0.4
0.3
0.2
0.1
0.0
Untreated
Empty Vector
Targeting dRNA-71

FIG.8B

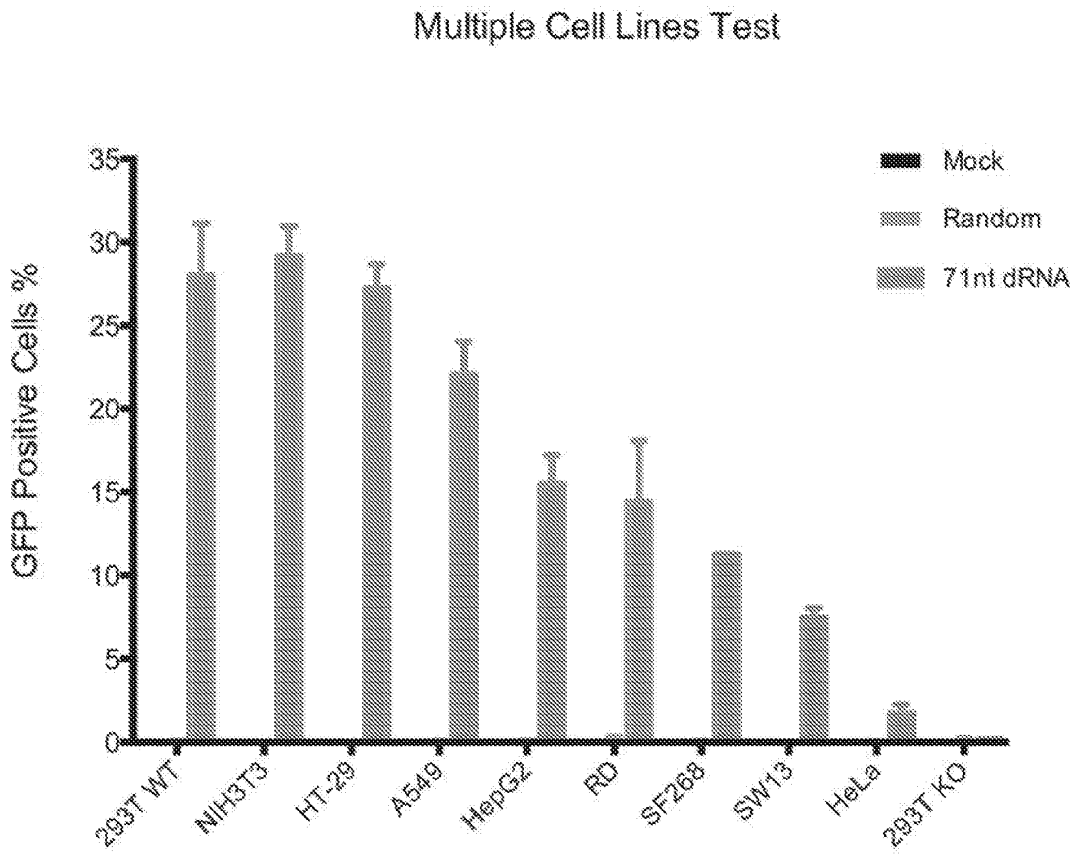

Multiple Cell Lines Test
GFP Positive Cells %
35
30
25
20
15
10
5
0
Mock
Random
71nt dRNA
293T WT
NIH3T3
HT-29
A549
HepG2
RD
SF268
SW13
HeLa
293T KO

FIG.9

FIG.10A

FIG.10B

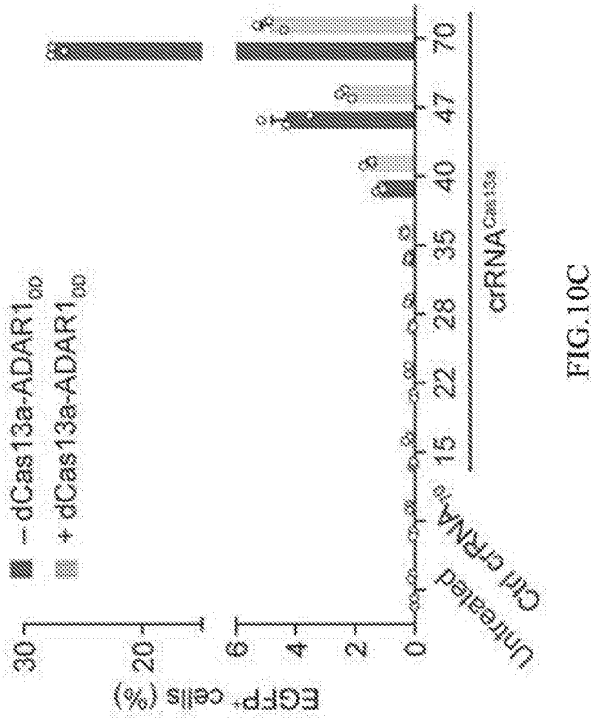


FIG.10C

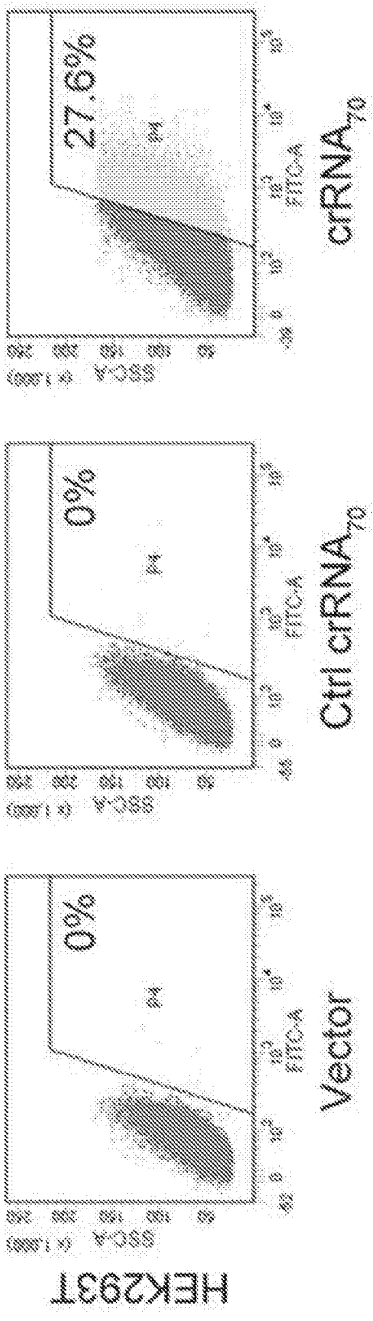


FIG.10D

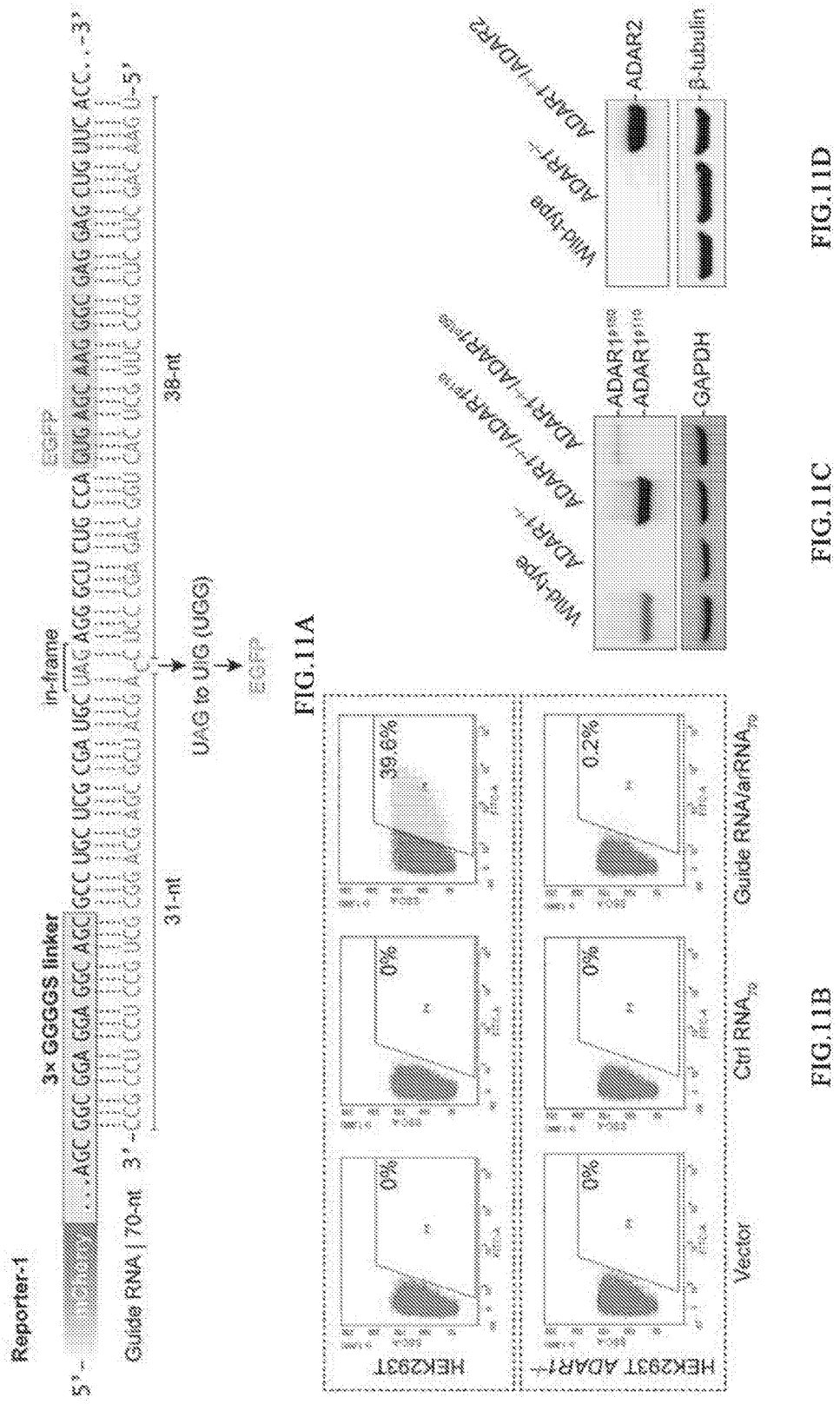


FIG.11A FIG.11B FIG.11C FIG.11D

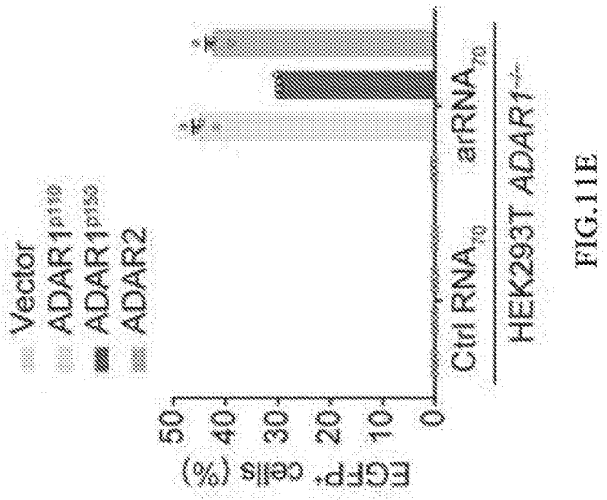


FIG.11E

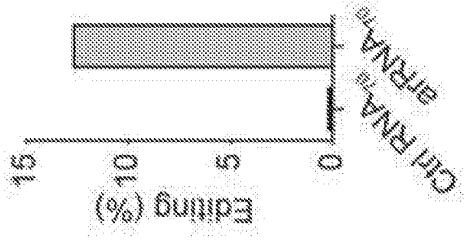


FIG.11G

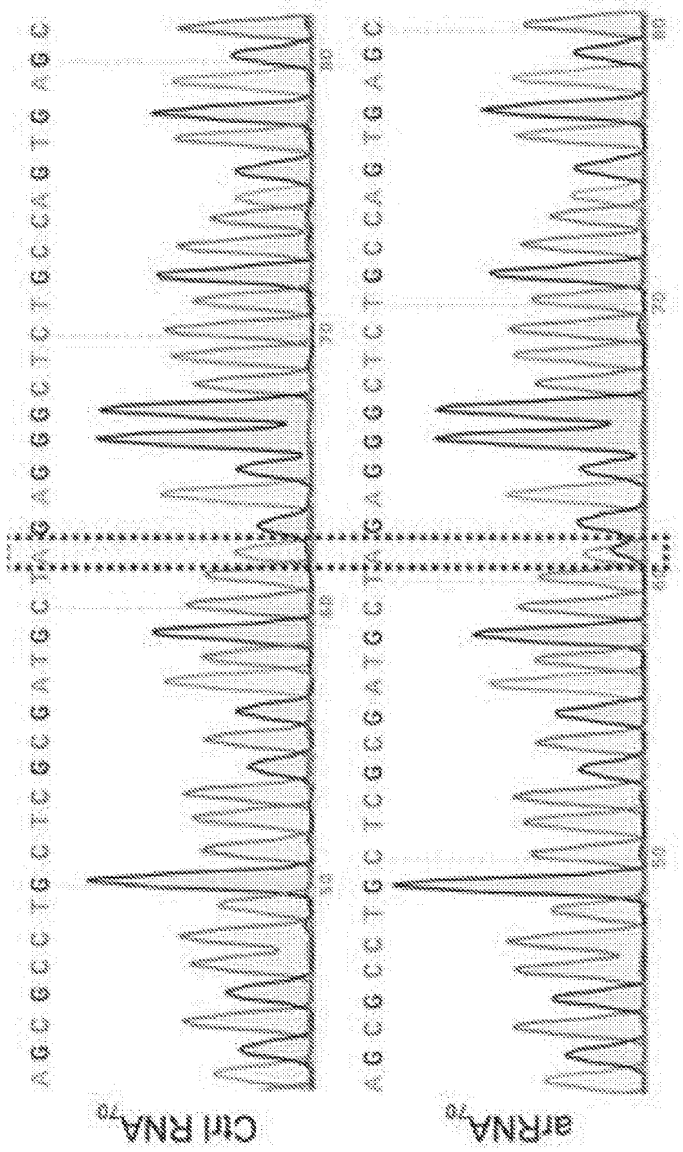


FIG.11F

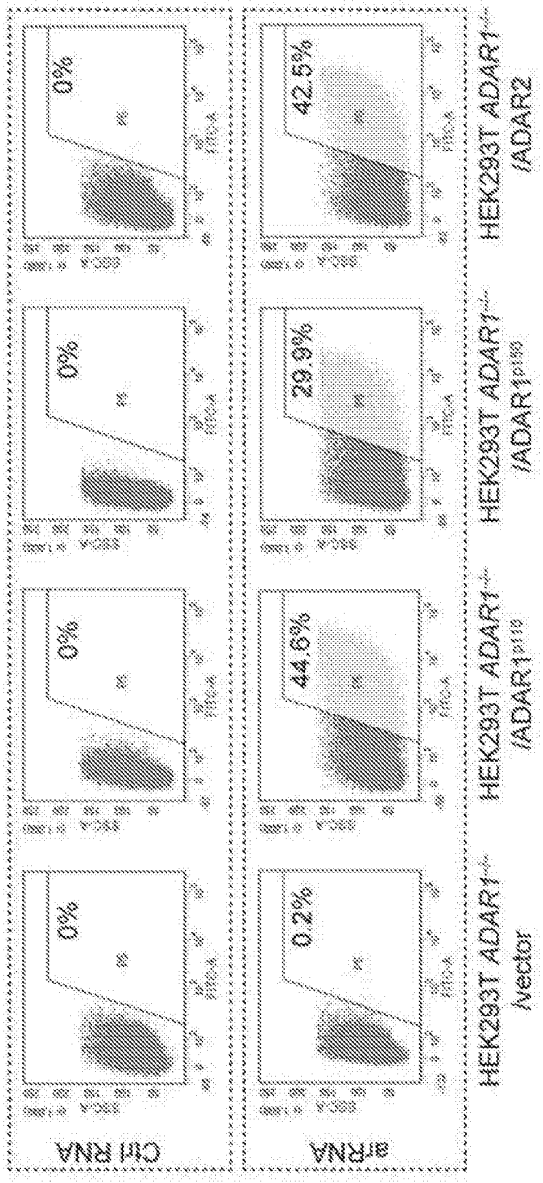


FIG.12B

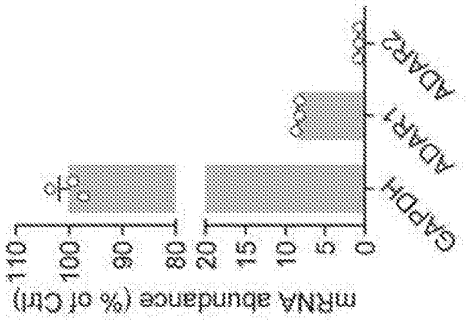


FIG.12A

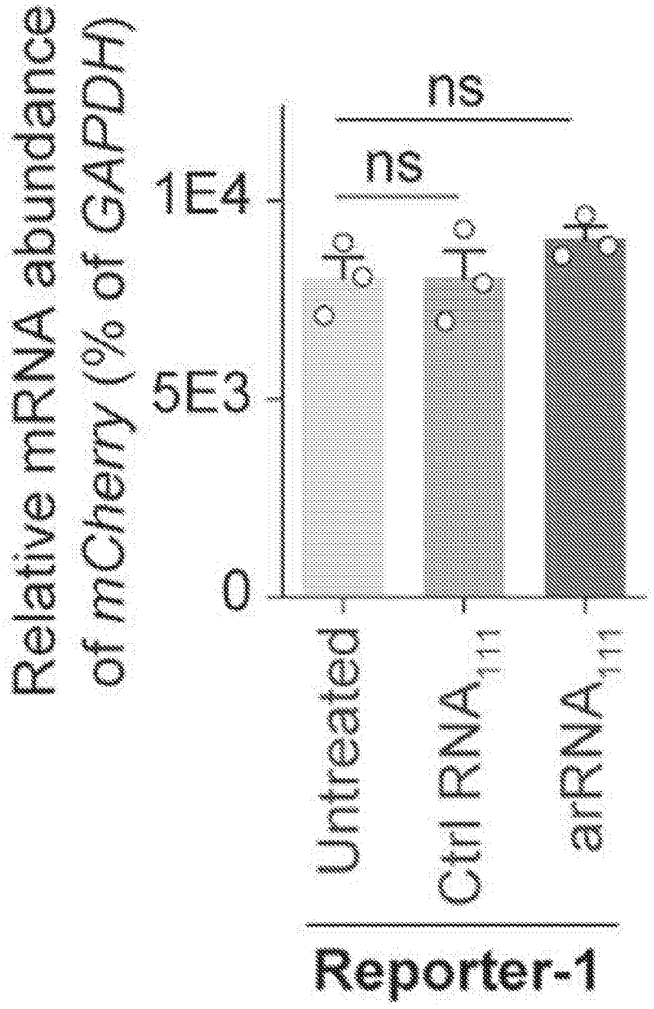

Relative mRNA abundance
of mCherry (% of GAPDH)
ns
ns
1E4
5E3
0
Untreated
Ctrl RNA111
arRNA111
Reporter-1

FIG.13

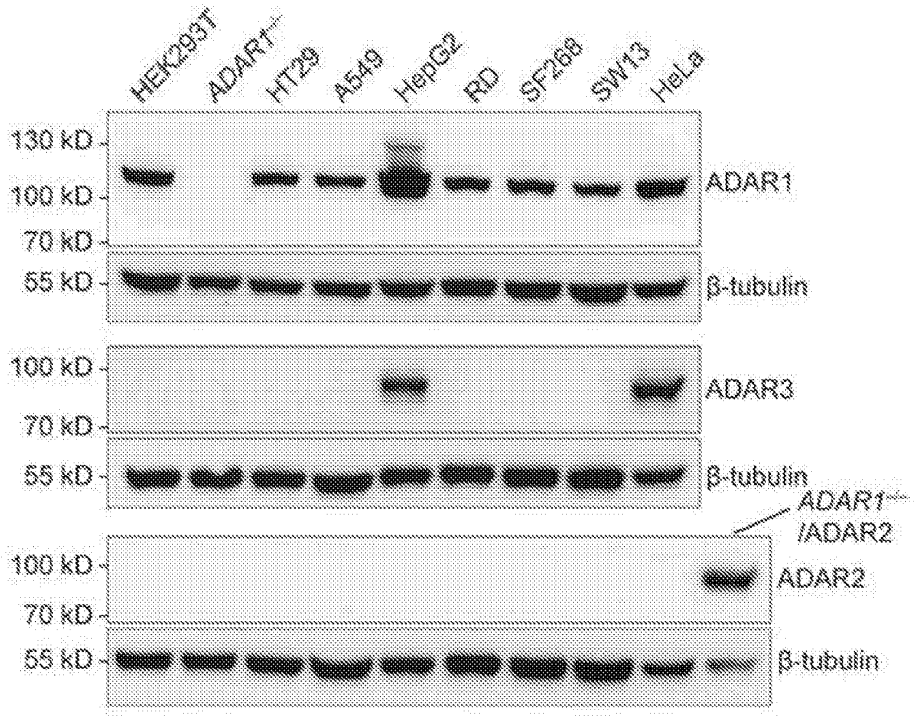


FIG.14A

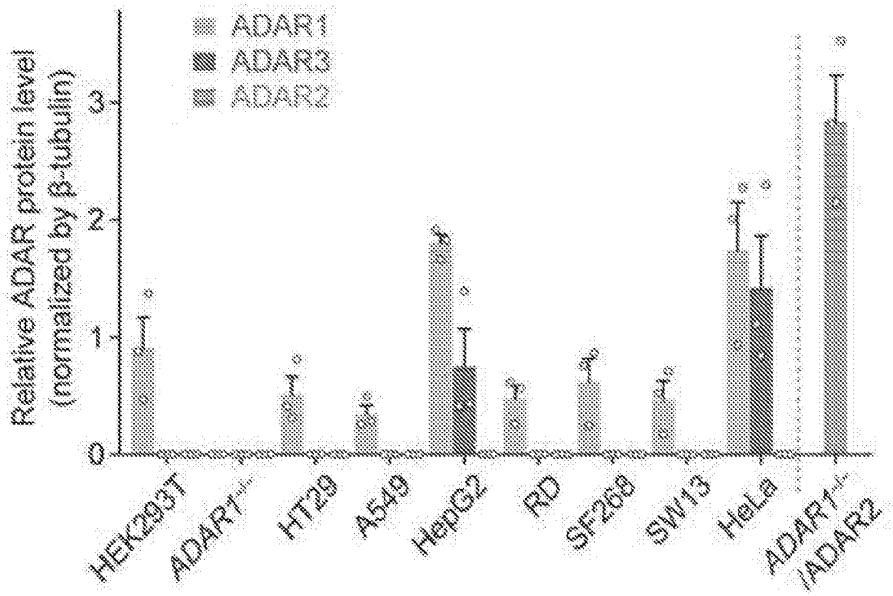


FIG.14B

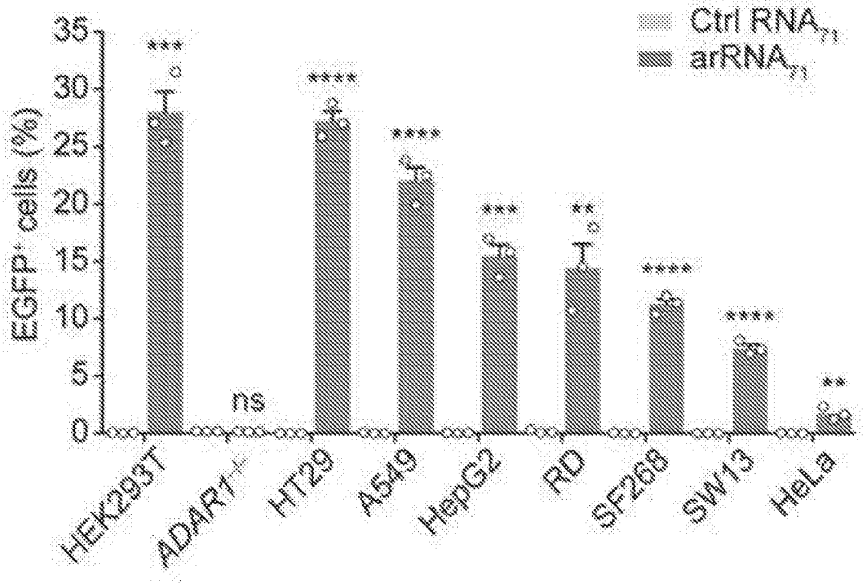


FIG.14C

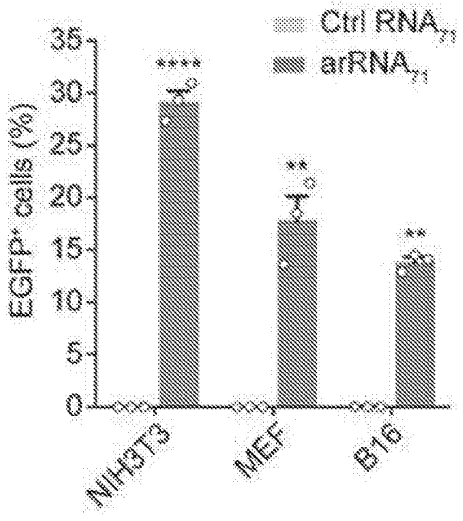


FIG.14D

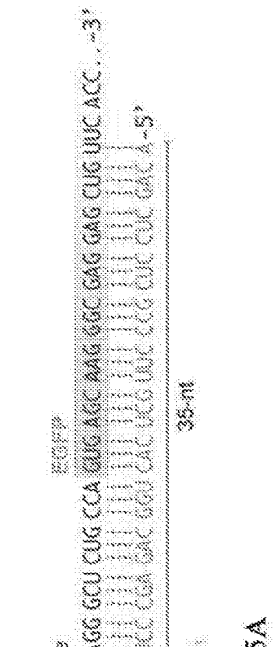


FIG.15A

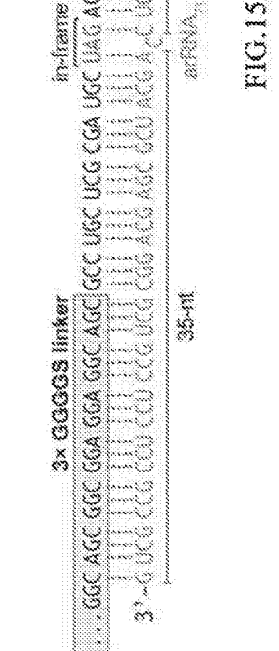


FIG.15B

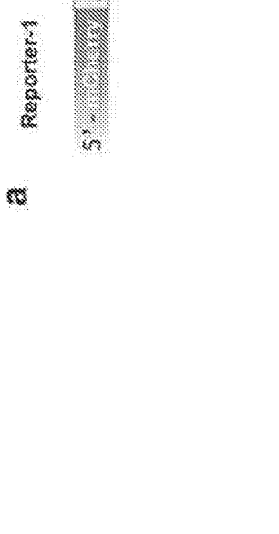


FIG.15C

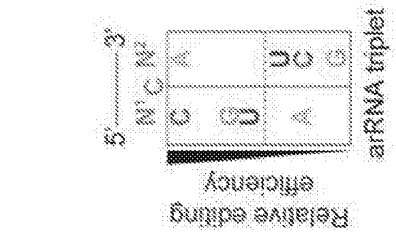


FIG.16C

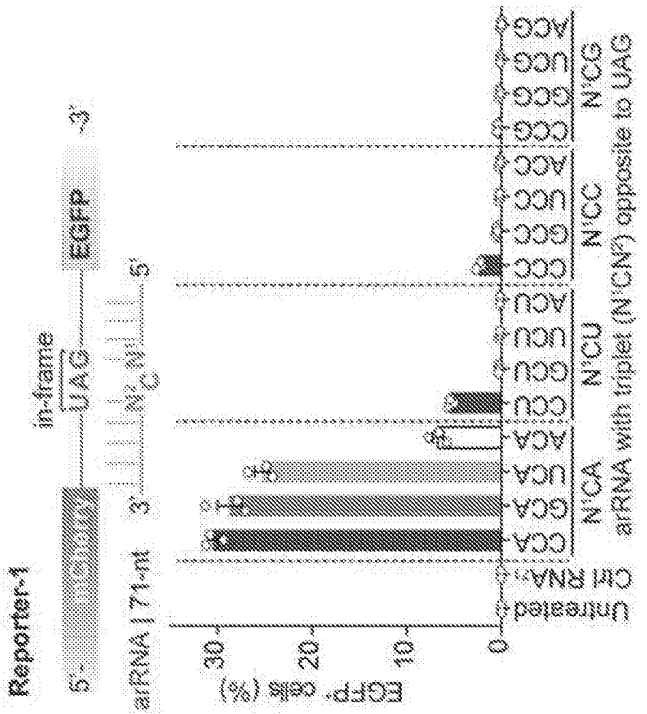


FIG.16B

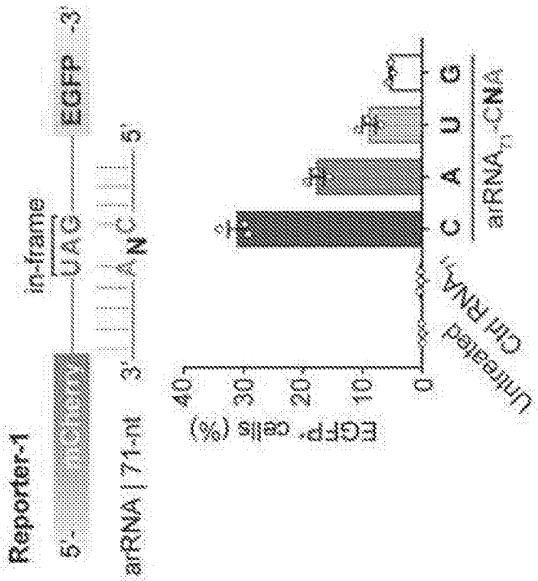


FIG.16A

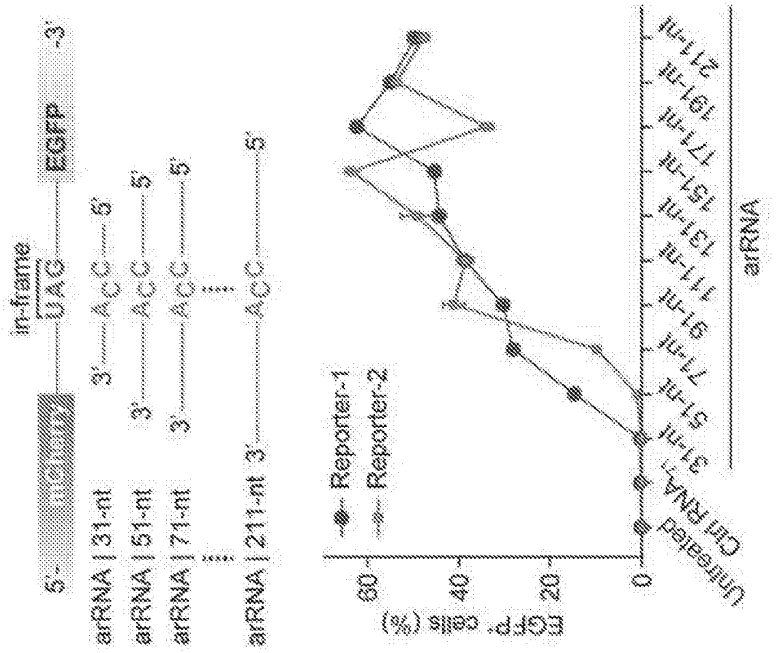


FIG.16D

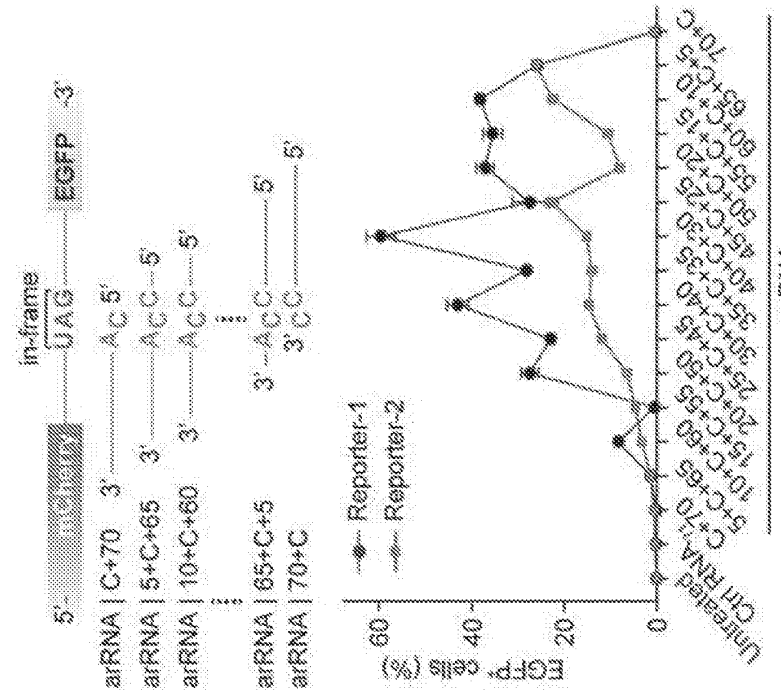


FIG.16E

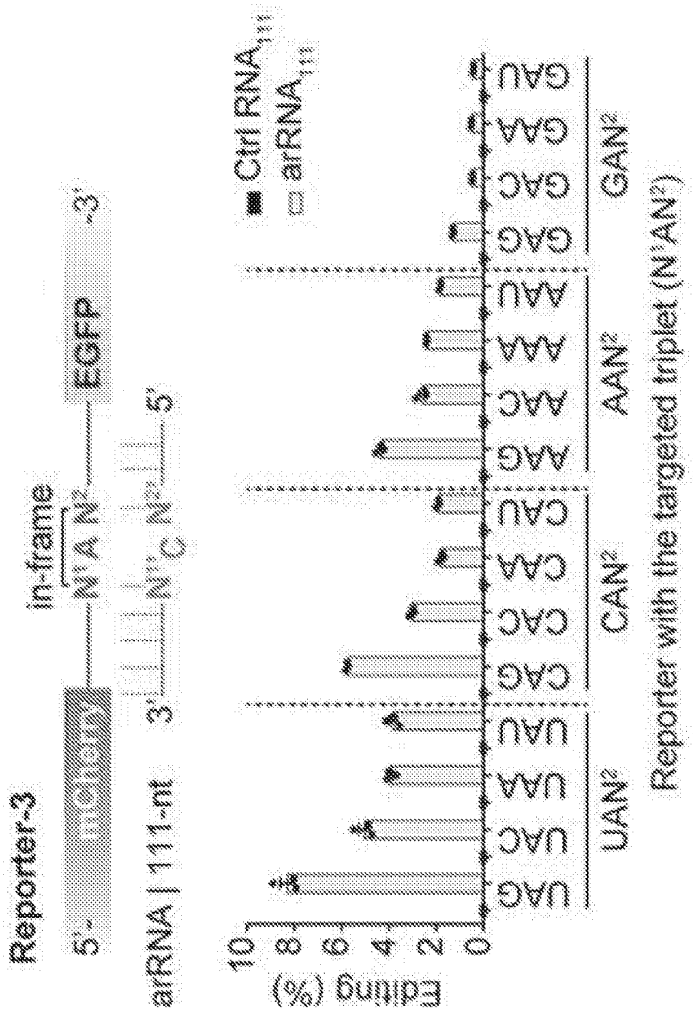


FIG.16F

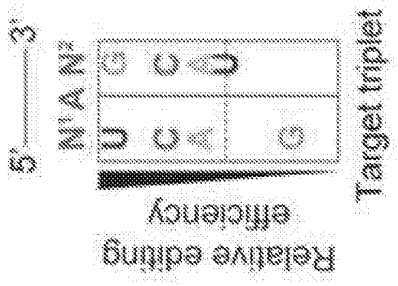


FIG.16G

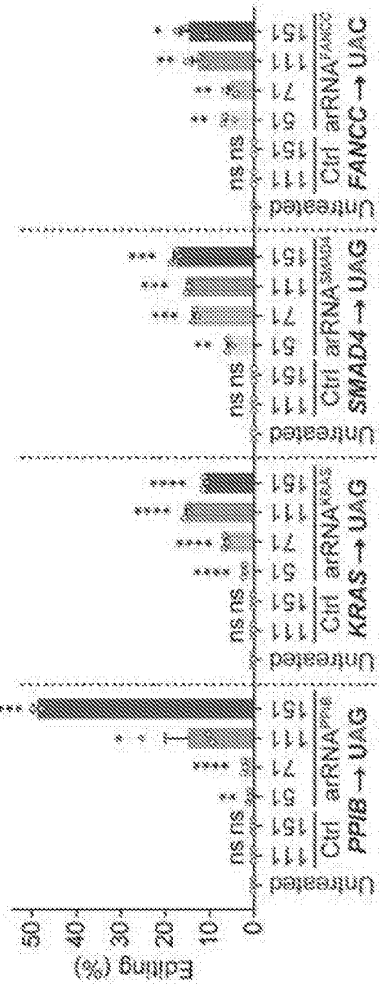


FIG.17B

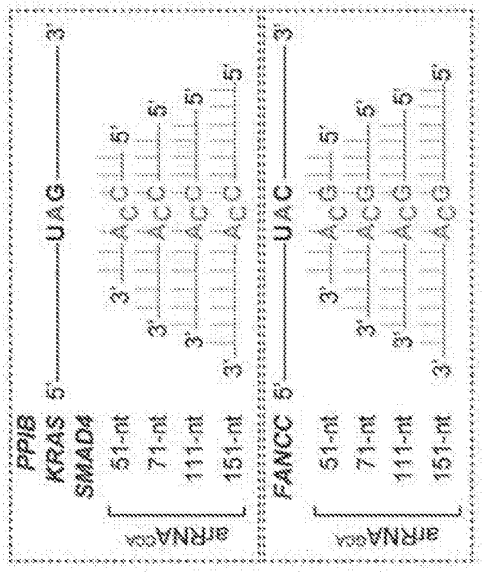


FIG.17A

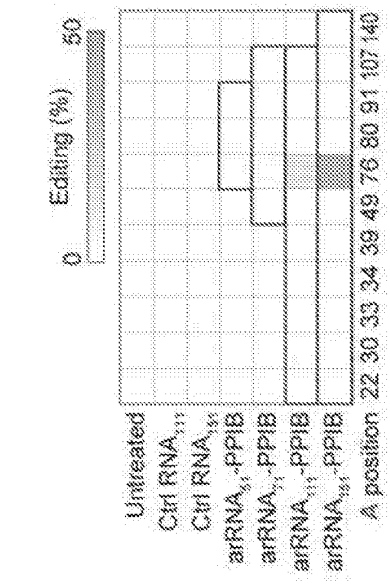


FIG.17F

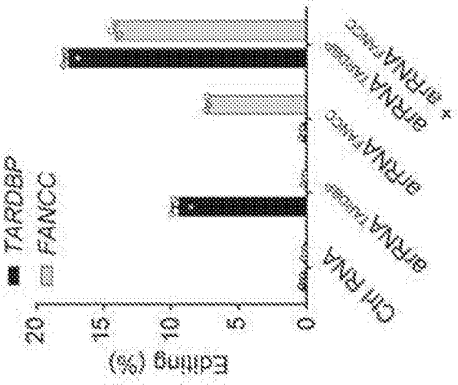
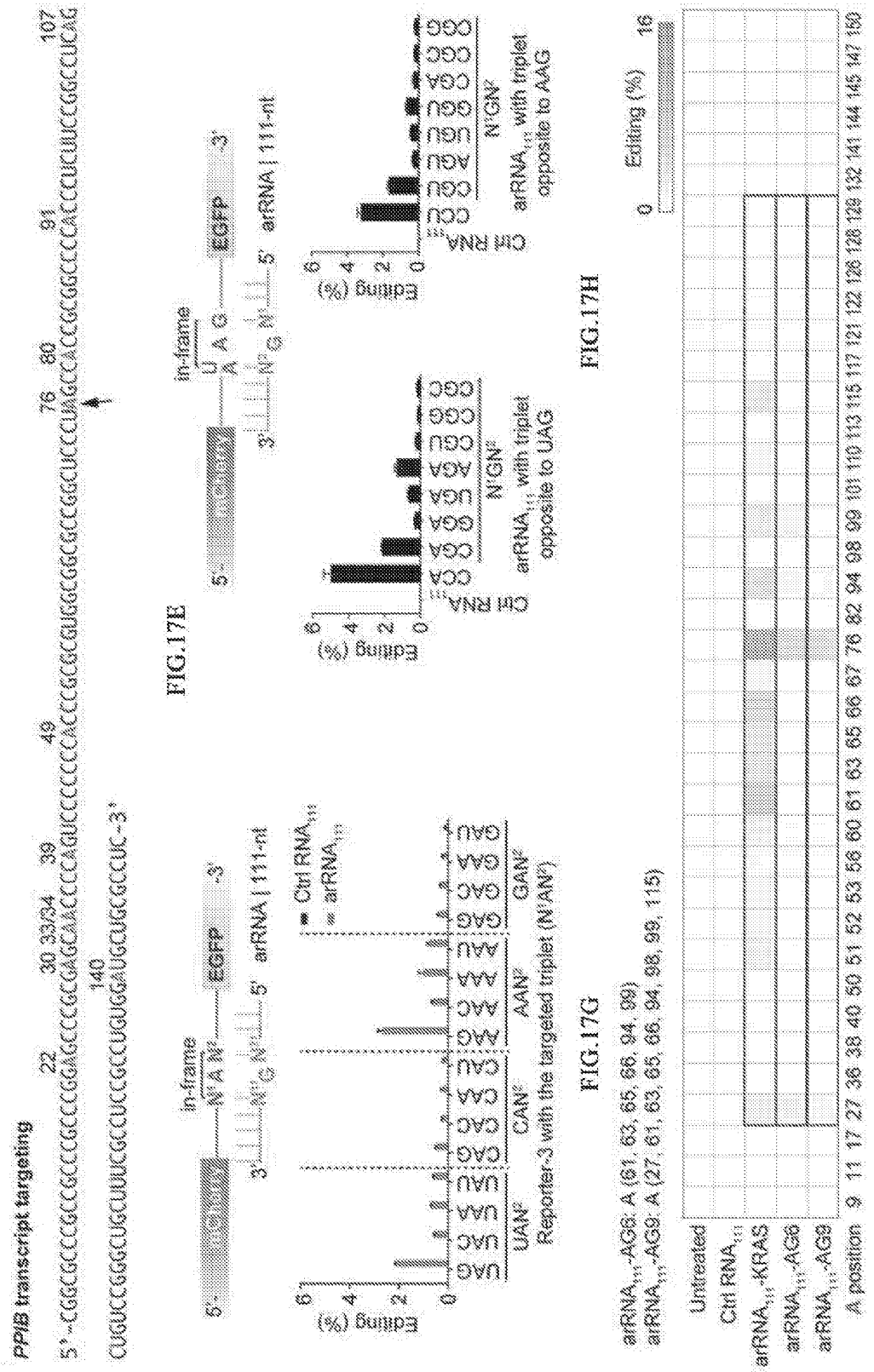


FIG.17D

FIG.17C


PPIB transcript targeting
FIG.17E
FIG.17G
FIG.17H
FIG.17I
in-frame
EGFP
arRNA | 111-nt
Ctrl RNA111
arRNA111
Editing (%)
arRNA111 with triplet opposite to UAG
arRNA111 with triplet opposite to AAG
Reporter-3 with the targeted triplet (N1AN2)
arRNA111-AG8: A (61, 63, 65, 66, 94, 99)
arRNA111-AG9: A (27, 61, 63, 65, 66, 94, 98, 99, 115)
Untreated
Ctrl RNA111
arRNA111-KRAS
arRNA111-AG8
arRNA111-AG9
A position

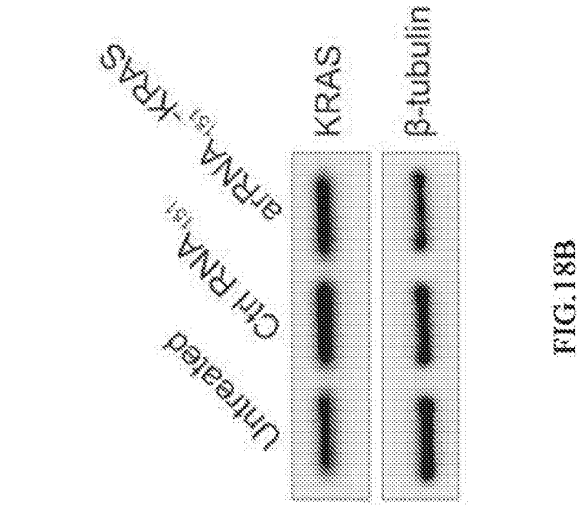


FIG.18B

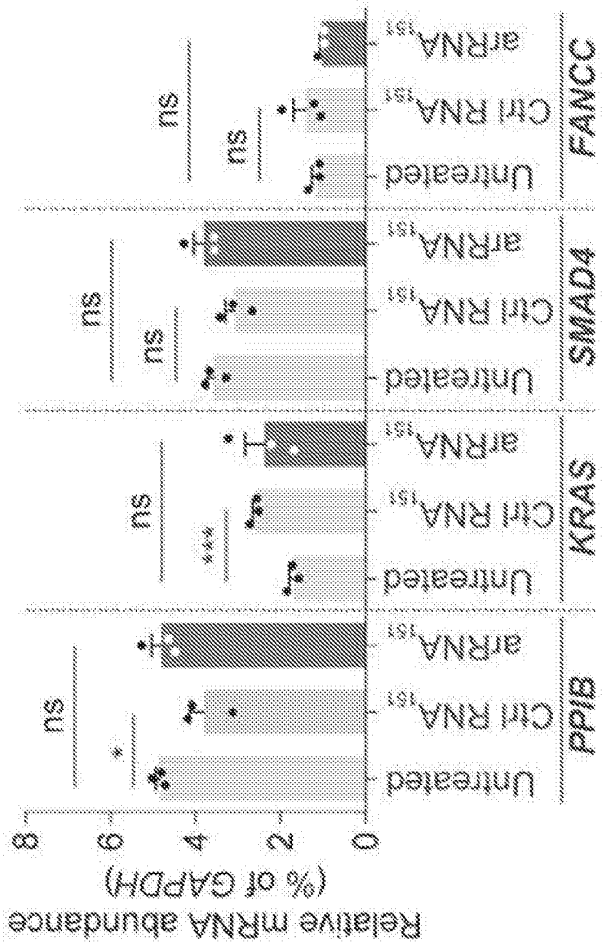


FIG.18A

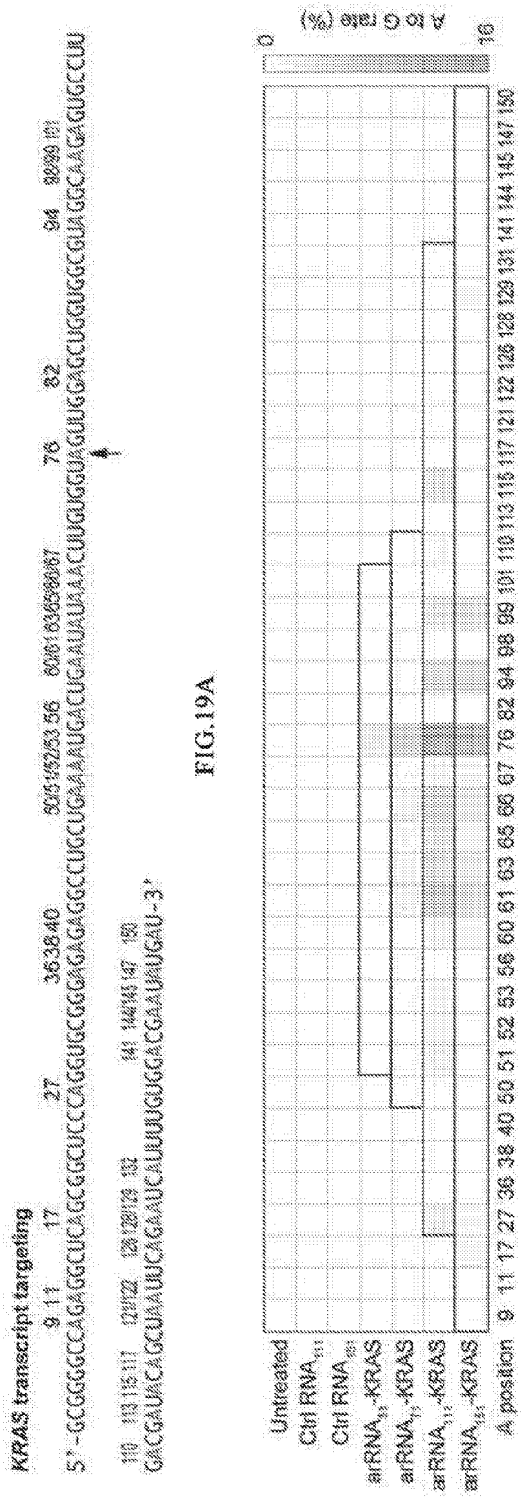


FIG.19A

FIG.19B

FIG.19C

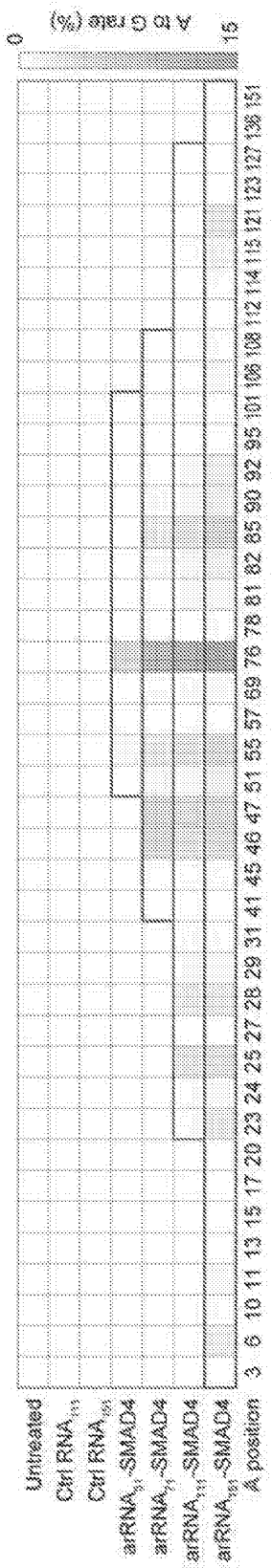


FIG.19D

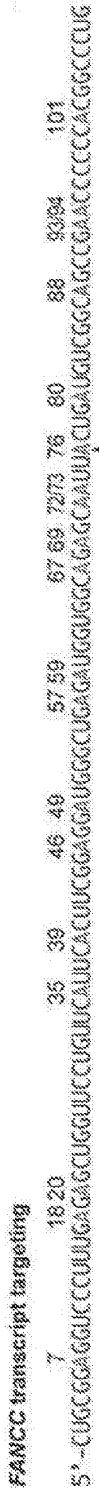


FIG.19E

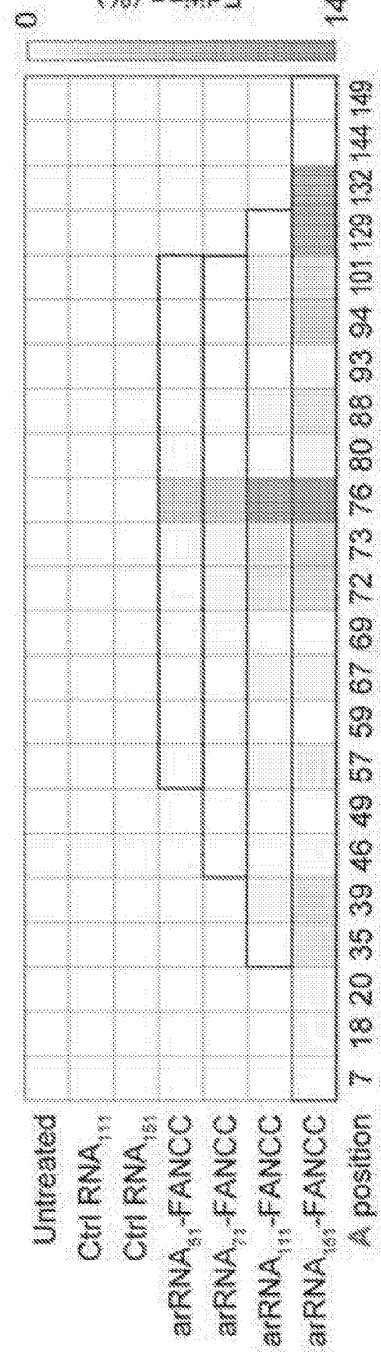


FIG.19F

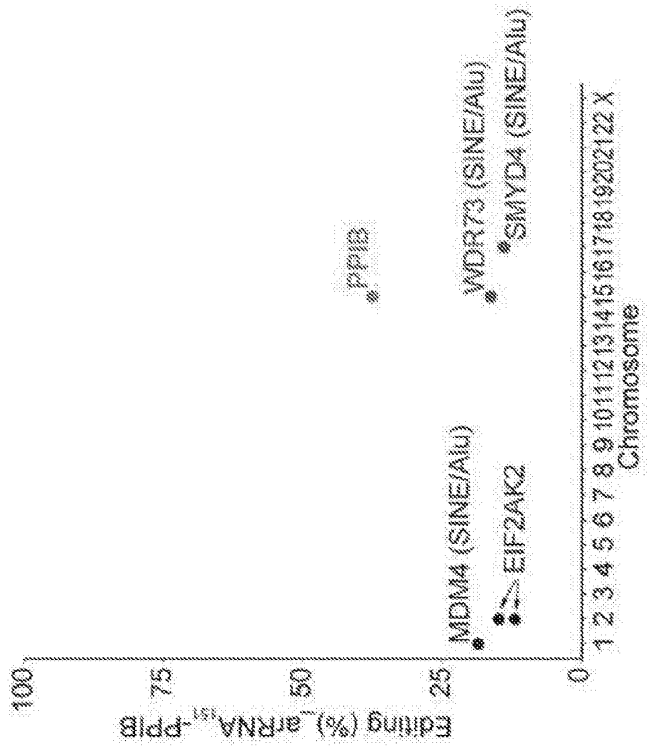


FIG.20B

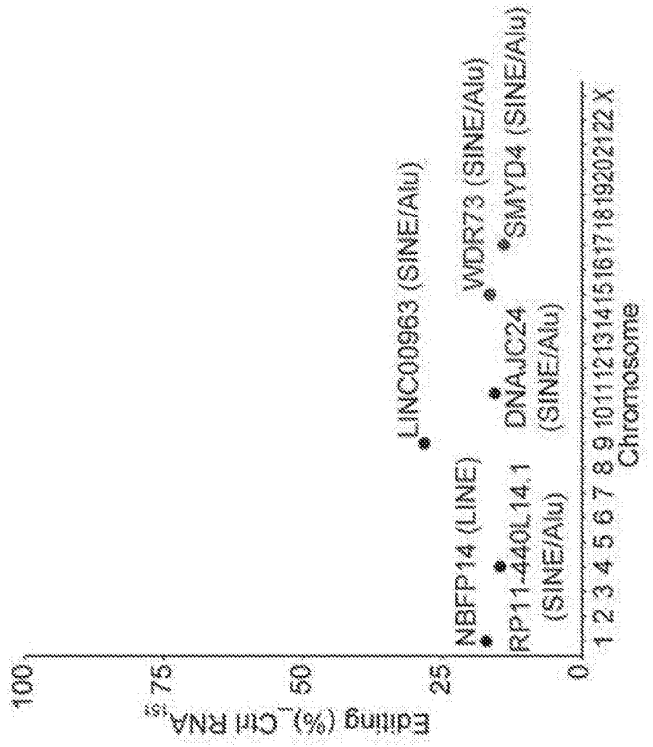


FIG.20A

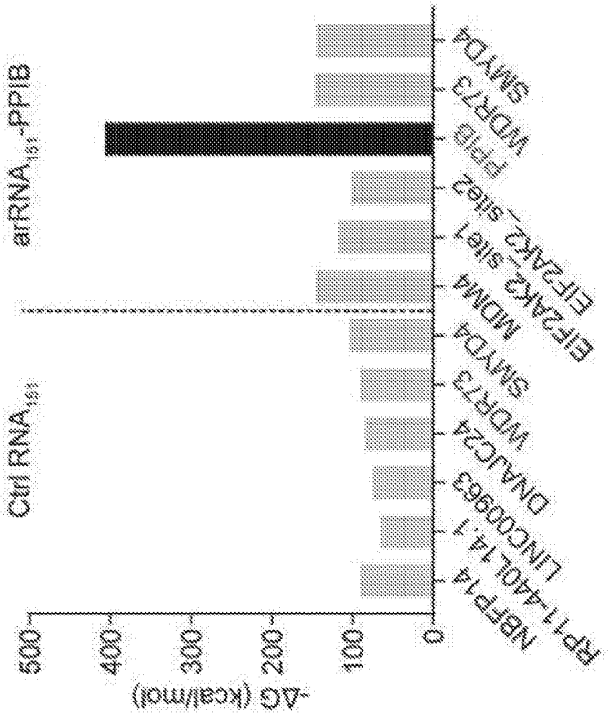


FIG.20C

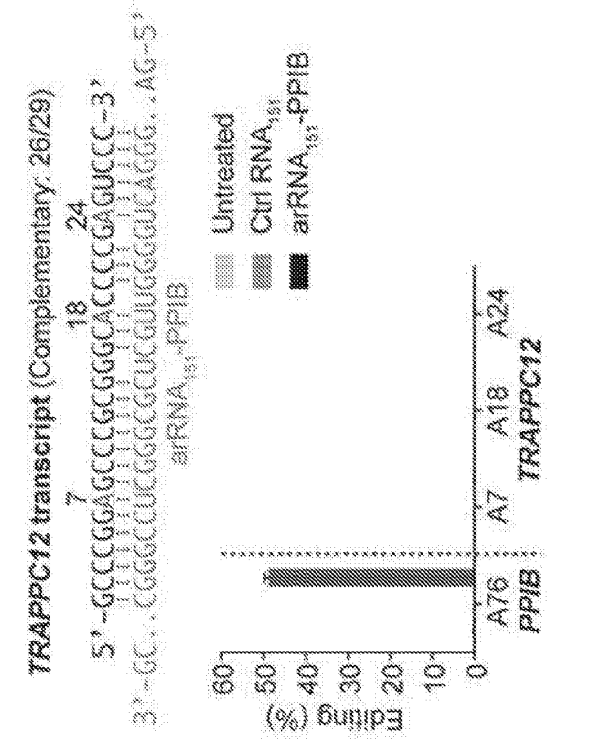


FIG.20D

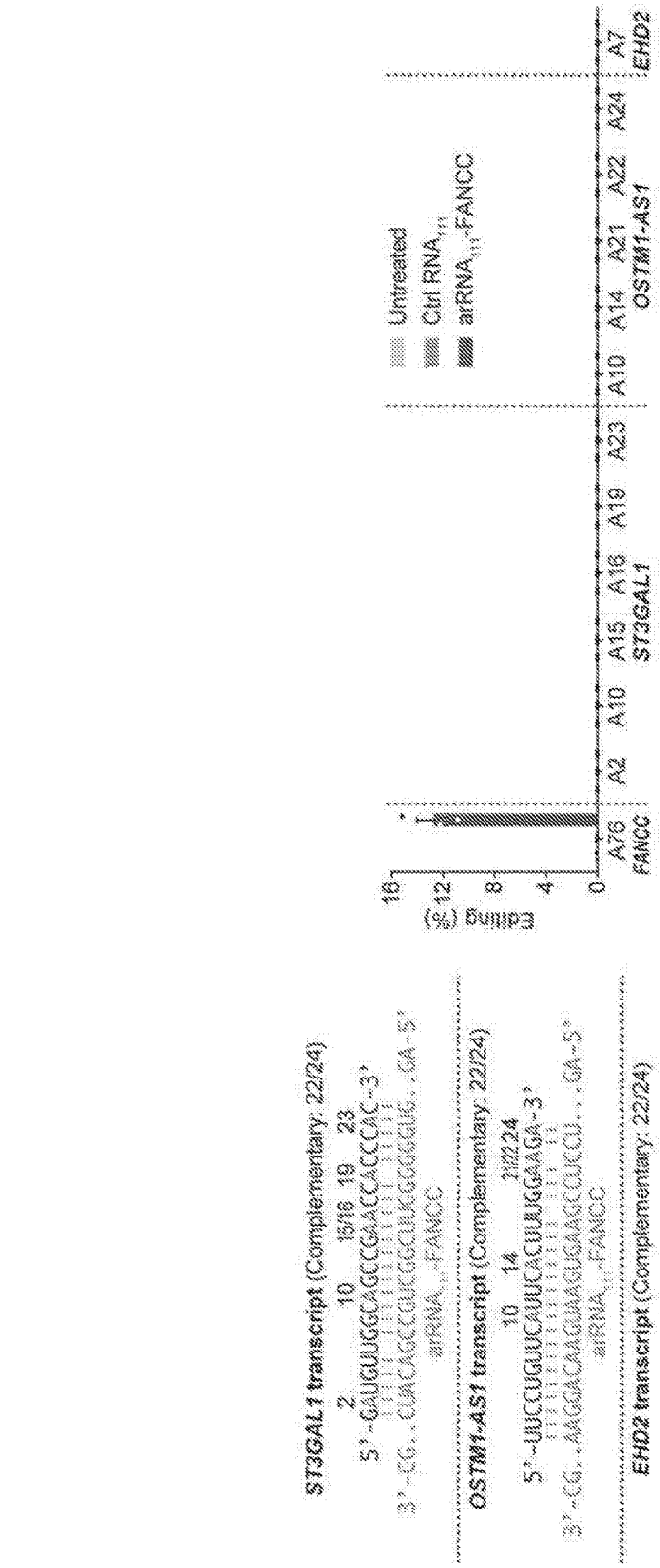


FIG.21A

FIG.21B

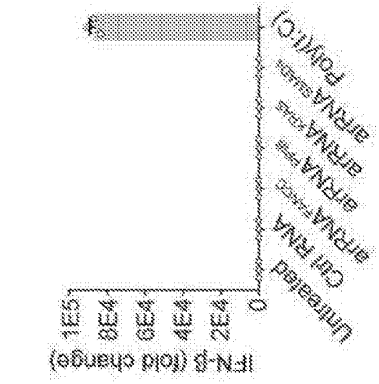


FIG.22E

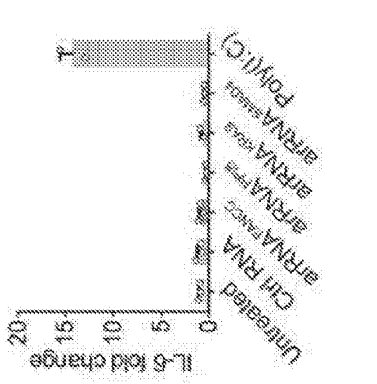


FIG.22F

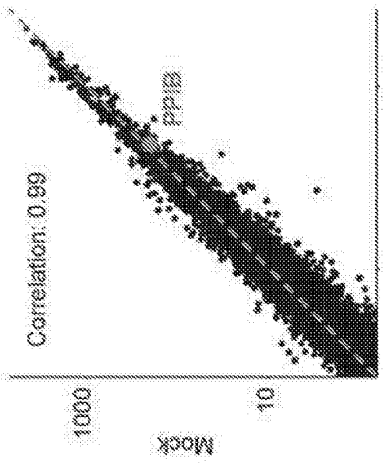


FIG.22C

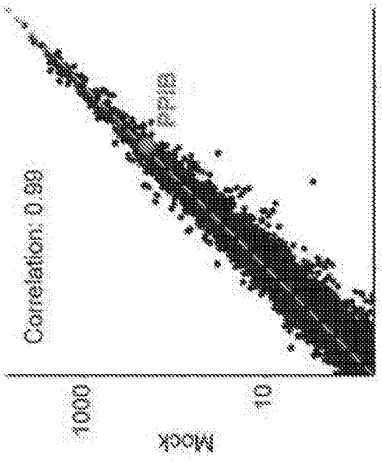


FIG.22D

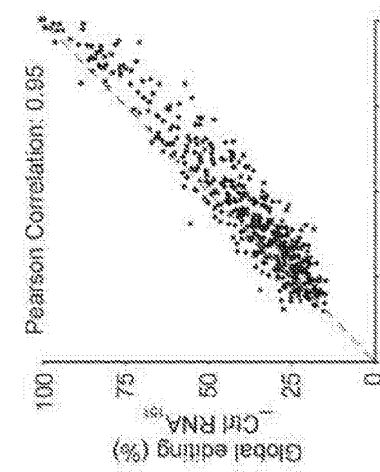


FIG.22A

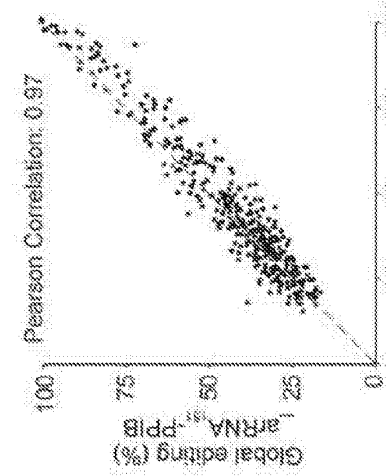


FIG.22B

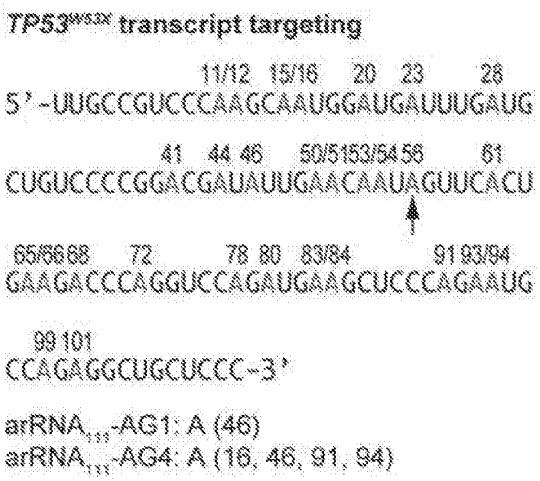


FIG.23A

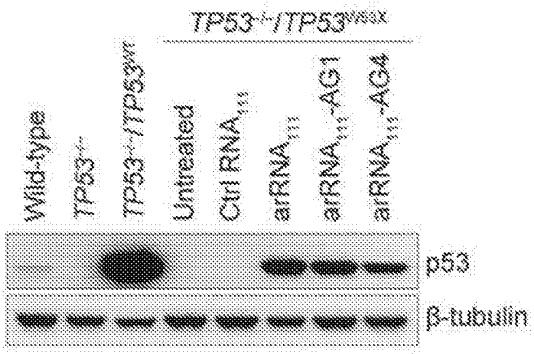


FIG.23C

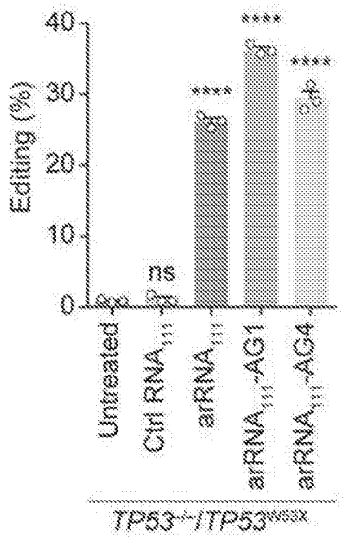


FIG.23B

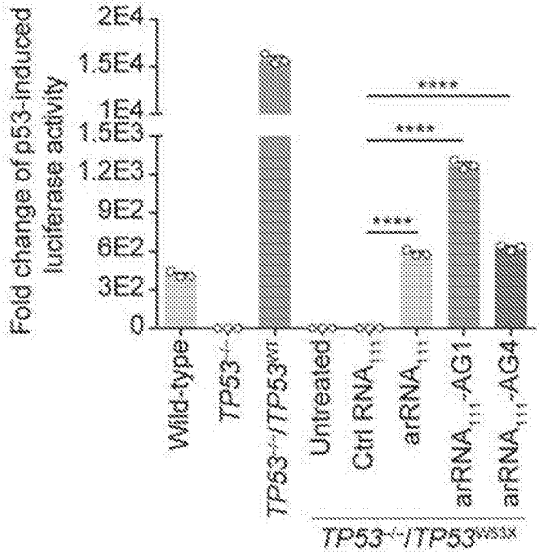
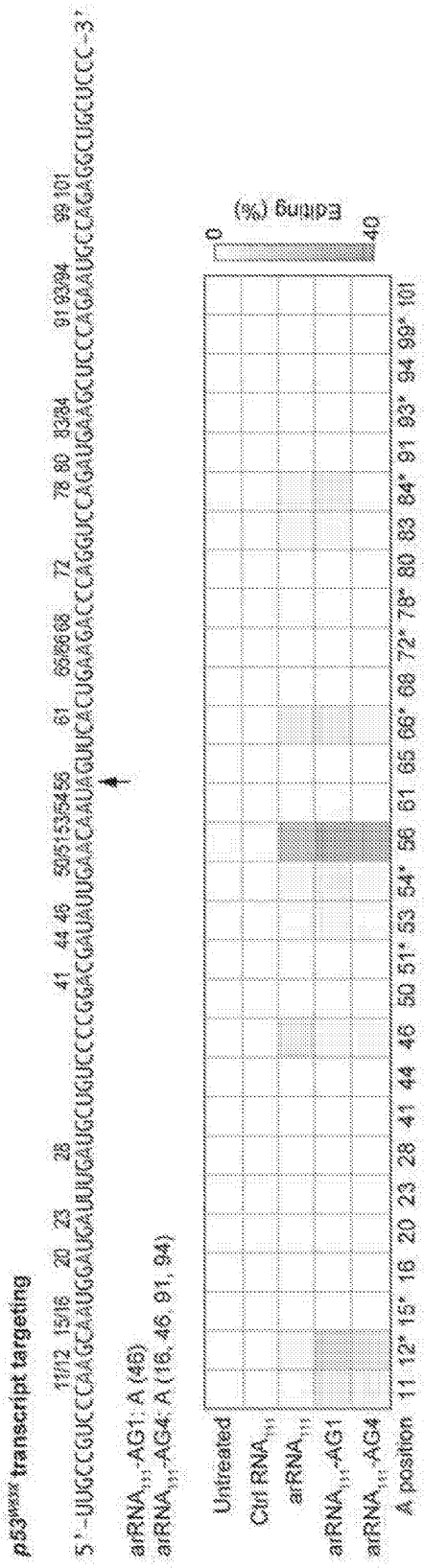


FIG.23D



*Adenosine sites undergoing A-to-I conversion result in synonymous mutations.

FIG.24

COL3A1 targeting
c.3833G>A
5' - CCCUAGAAACUGCAGACCUGAAAUUCUGCCAUCCUGAACUCAAGAGUGGAGAAUACUGGUUGACCCUAACCAAGGAUGCAAAUUGGAUCCUAUCAAGGUAUUCUGUAAUAUGGAAAC - 3'
3' -UCUAAGGUCGUCUGGACUUUAAGACGGUAGGACUUGAGUUCUCACCUAGGUUCCUGGGAUUGGGUUGGAUUCCUAGGAUAGACAUUAUACCUUUGCCUUAUACCUGUUUG-5'
55-nt
BMPR2 targeting
c.893G>A
5' - UGAUGGAGUACUAUCCCAAUGGAUCUUUAUUUAAGUCUCCACACAAGUGACUUGGUAAGCUCUUGCCGUCUUGGUCAUUCUGUUACUAGAGGACUGGCCUUAUCUUUCACACAGA - 3'
3' -CUCAAUACCUGAUAGGGUUACCUAGAAAUUCAUGCCUGAUUCACUGAACCAGAAUUCGUCUUCGAUUCAAUGACAAUAAGACAGAAUGAUAGAAAGUGUCUGAAAUAAAGUG-5'
55-nt
AHI1 targeting
c.2174G>A
5' - UCCAUCCAGCUGUAAGAGAGCUAGUAGUUACAGGAUGCUAUGAUUCCAUGAUACGGAUAUUGAAAGUUGAGAUGAGAGAAGAUUCUGCCGACAGUUUGACGUUCACAAAAG - 3'
3' -GGUCGACAAUCGUCAUUCUCUAUCAUGAUACUAUGCCUAUA CUUUCAACGUCUACUCUUCUUAAGCUGUCAAACUGCAAGUGUUUUC-5'
55-nt
PANCC targeting
c.1617G>A
5' - UGAUCAGGCACCUUCUCCUCAACUUCCUGCUCUGGGCUCCUGGAGGCCACACGAUCGCCUAGGAUGUCAUCACCUGAUGGCUCACACUGUGAGAUAACUCACCAGAUCAUUGGCUUUCU- 3'
3' -UCCUAGUGGAGGAGUUGAAGGACGAGACGACUAGCGGAUCCUACAGUAGUGUGACACUCUAUUGAGUGGUCUAGUGUCACCGAGUAGUAACUCUAUGAGGUCUAGUAAAGA-5'
55-nt
MYBPC3 targeting
c.3293G>A
5' - GGGGUCUUAAUGUGGCUCUGGAGUGGAAGCCACCCCAGGAUGUCUGGCAACACGGAGCUCUAGGGGUACACAGUGCAGAAAGCCGACACAAGAAGACCAUGGAGUGGUUCACCGUCUUGGAGCA - 3'
3' -CAAUUAUCCCAAGGUCUACACCUUCGUGCCUCAGCCCCUUGUGCCUCAGAUCCCCAUGUGUUUCACCUCAUCGUCUGUUCUGGUACUCACCAAGUGGCAGAAC-5'
55-nt
IL2RG targeting
c.710G>A
5' - AACGCUACACGUUUCGUGUUCCGAGCCGCUUUAACCCACUCUGUGGAAGUGCUCAGCAUUGAGUGAAUGGAGCCACCCAAUCCACGUGGGGAGCAAUACUUCAAAAGAGAAUCCUUUCCU- 3'
3' -AUGCGAUGUGCAAGGCUCGGCGAAAUUGGGUGAGACUCACGUAACUCGUAGGUGCACUCGGUUACCUCGUUAUGUGAAGUUUUCUCUUAGGAAAGGAAAGGACUUAGGA-5'
55-nt

FIG.25

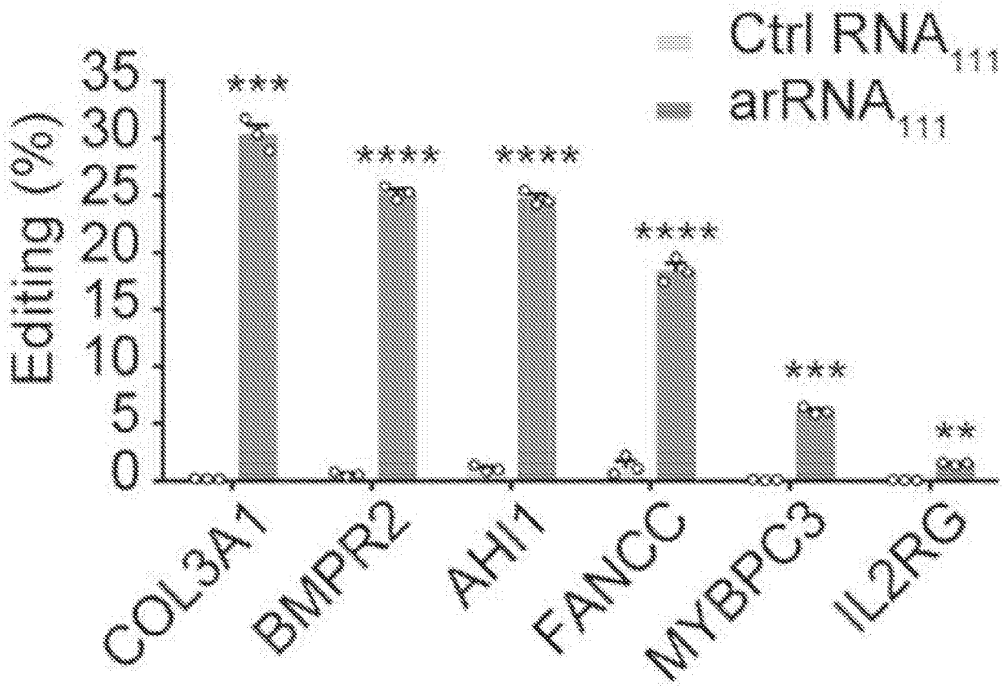

Ctrl RNA111
arRNA111
Editing (%)
35
30
25
20
15
10
5
0
***
****
****
****
***
**
COL3A1
BMPR2
AHI1
FANCC
MYBPC3
IL2RG

FIG.26

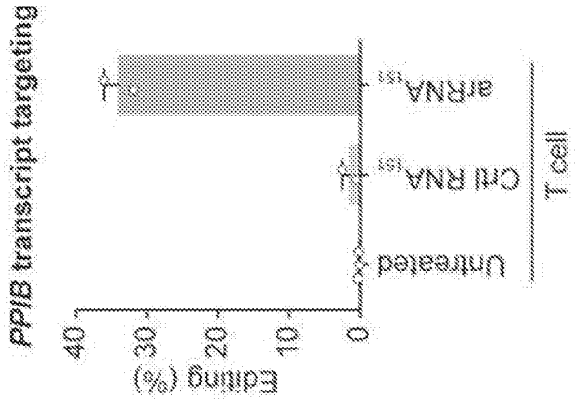


FIG.27C

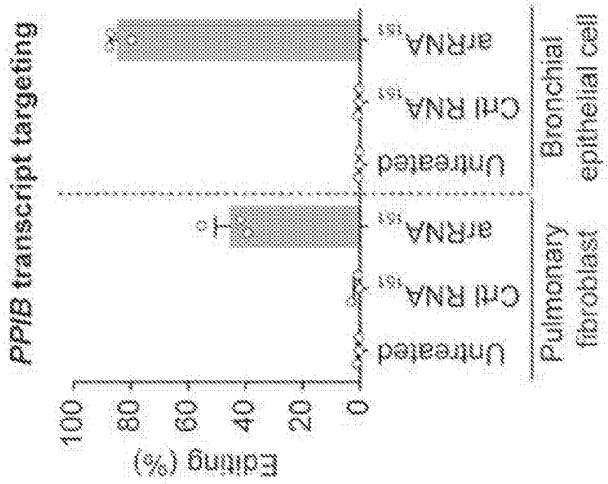


FIG.27B

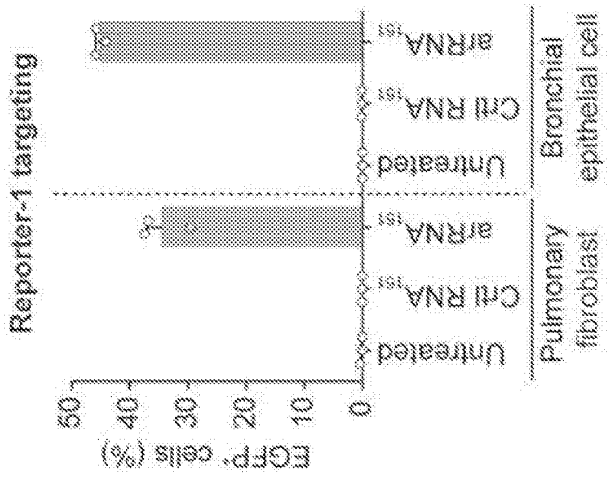


FIG.27A

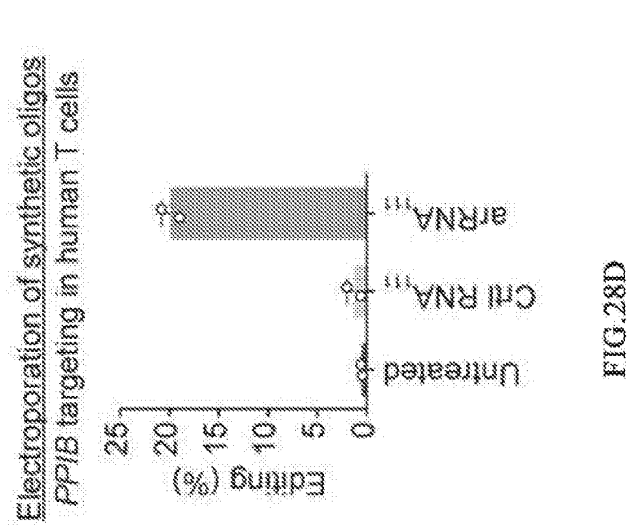


FIG.28A

FIG.28B

FIG.28D

FIG.28C

FIG.29A

FIG.29B

FIG.29C

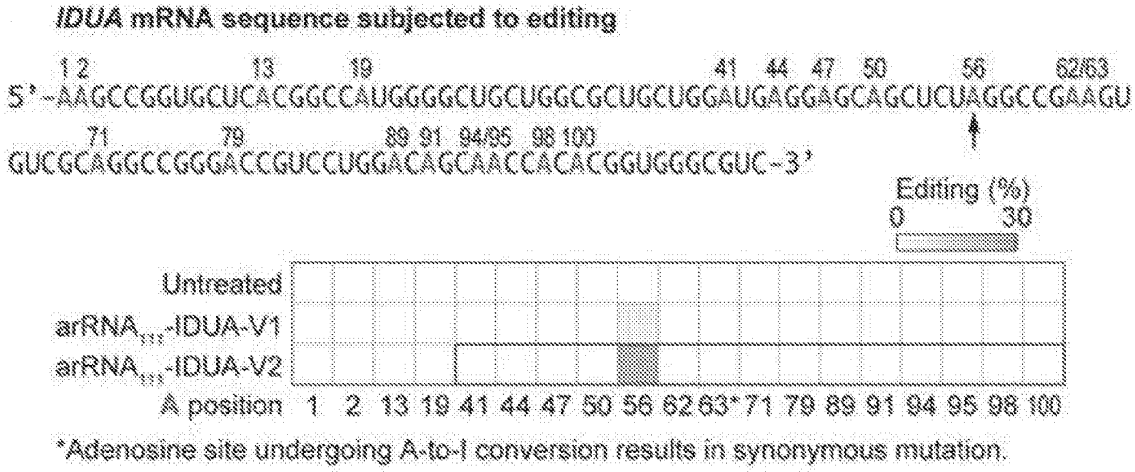


FIG.29D

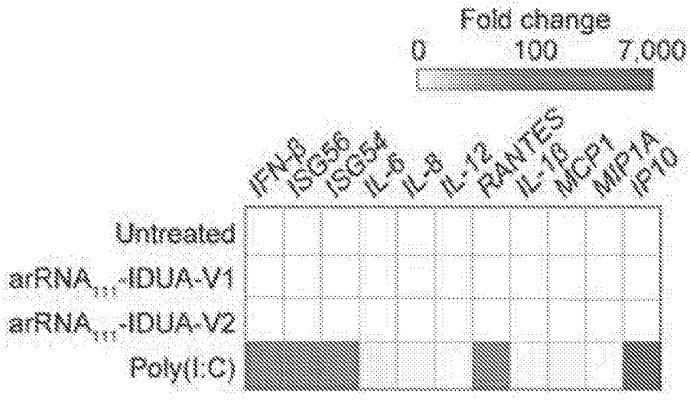


FIG.29E

Reporter-1:



5'-

ATGGTGAGCAAGGGCGAGGAGGATAACATGGCCATCATCAAGGAGTTCATGCGCTTCAAGGTGCA
CATGGAGGGCTCCGTGAACGGCCACGAGTTCGAGATCGAGGGCGAGGGCGAGGGCCGCCCCTAC
GAGGGCACCCAGACCGCCAAGCTGAAGGTGACCAAGGGTGGCCCCCTGCCCTTCGCCTGGGACAT
CCTGTCCCCTCAGTTCATGTACGGCTCCAAGGCCTACGTGAAGCACCCCGCCGACATCCCCGACTA
CTTGAAGCTGTCCTTCCCCGAGGGCTTCAAGTGGGAGCGCGTGATGAACTTCGAGGACGGCGGCG
TGGTGACCGTGACCCAGGACTCCTCCCTGCAGGACGGCGAGTTCATCTACAAGGTGAAGCTGCGC
GGCACCAACTTCCCCTCCGACGGCCCCGTAATGCAGAAGAAGACCATGGGCTGGGAGGCCTCCTC
CGAGCGGATGTACCCCGAGGACGGCGCCCTGAAGGGCGAGATCAAGCAGAGGCTGAAGCTGAAG
GACGGCGGCCACTACGACGCTGAGGTCAAGACCACCTACAAGGCCAAGAAGCCCGTGCAGCTGCC
CGGCGCCTACAACGTCAACATCAAGTTGGACATCACCTCCCACAACGAGGACTACACCATCGTGGA
ACAGTACGAACGCGCCGAGGGCCGCCACTCCACCGGCGGCATGGACGAGCTGTACAAG *CTGCAG*
GGCGGAGGAGGCAGC GGCGGAGGAGGCAGC GGCGGAGGAGGCAGC
GCCTGCTCGCGATGCTAGAGGGCTCTGCCA
GTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAAC
GGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTC
ATCTGCACCACCGGCAAGCTGCCCGTGCCCTGGCCCACCCTCGTGACCACCCTGACCTACGGCGTGCAGT
GCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGT
CCAGGAGCGCACCATCTTCTTCAAGGACGACGGCAACTACAAGACCCGCGCCGAGGTGAAGTTCGAGGG
CGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCA
CAAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAA
GGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAA
CACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCTGAGC
AAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTC
GGCATGGACGAGCTGTACAAGTAA-3'

FIG.30A

Reporter-2:



5'-

ATGGTGAGCAAGGGCGAGGAGGATAACATGGCCATCATCAAGGAGTTCATGCGCTTCAAGGTGCA
CATGGAGGGCTCCGTGAACGGCCACGAGTTCGAGATCGAGGGCGAGGGCGAGGGCCGCCCCTAC
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CCTGTCCCCTCAGTTCATGTACGGCTCCAAGGCCTACGTGAAGCACCCCGCCGACATCCCCGACTA
CTTGAAGCTGTCCTTCCCCGAGGGCTTCAAGTGGGAGCGCGTGATGAACTTCGAGGACGGCGGCG
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CGAGCGGATGTACCCCGAGGACGGCGCCCTGAAGGGCGAGATCAAGCAGAGGCTGAAGCTGAAG
GACGGCGGCCACTACGACGCTGAGGTCAAGACCACCTACAAGGCCAAGAAGCCCGTGCAGCTGCC
CGGCGCCTACAACGTCAACATCAAGTTGGACATCACCTCCCACAACGAGGACTACACCATCGTGGA
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GGCGGAGGAGGCAGC GGCGGAGGAGGCAGC GGCGGAGGAGGCAGC
AGAAGGTATACACGCCCGGAAGAATCTGTAGAGATCCCCGGTCGCCACC
GTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAAC
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GCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGT
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CAAGCTGGAGTACAACTACAACAGCCACAACGTCTATATCATGGCCGACAAGCAGAAGAACGGCATCAA
GGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAA
CACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCTGAGC

FIG.30B

AAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTC
GGCATGGACGAGCTGTACAAGTAA-3'

Reporter-3:



5'-
ATGGTGAGCAAGGGCGAGGAGGATAACATGGCCATCATCAAGGAGTTCATGCGCTTCAAGGTGCACATG
GAGGGCTCCGTGAACGGCCACGAGTTCGAGATCGAGGGCGAGGGCGAGGGCCGCCCCTACGAGGGCAC
CCAGACCGCCAAGCTGAAGGTGACCAAGGGTGGCCCCCTGCCCTTCGCCTGGGACATCCTGTCCCCTCAG
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CCTCCCTGCAGGACGGCGAGTTCATCTACAAGGTGAAGCTGCGCGGCACCAACTTCCCCTCCGACGGCCC
CGTAATGCAGAAGAAGACCATGGGCTGGGAGGCCTCCTCCGAGCGGATGTACCCCGAGGACGGCGCCCT
GAAGGGCGAGATCAAGCAGAGGCTGAAGCTGAAGGACGGCGGCCACTACGACGCTGAGGTCAAGACCA
CCTACAAGGCCAAGAAGCCCGTGCAGCTGCCCGGCGCCTACAACGTCAACATCAAGTTGGACATCACCT
CCCACAACGAGGACTACACCATCGTGGAACAGTACGAACGCGCCGAGGGCCGCCACTCCACCGGCGGCA
TGGACGAGCTGTACAAG CTGCAG ***GGCGGAGGAGGCAGC***
GCCTGCTCGCGATGCTAGAGGGCTCTGCCA
GTGAGCAAGGGCGAGGAGCTGTTCACCGGGGTGGTGCCCATCCTGGTCGAGCTGGACGGCGACGTAAAC
GGCCACAAGTTCAGCGTGTCCGGCGAGGGCGAGGGCGATGCCACCTACGGCAAGCTGACCCTGAAGTTC
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GCTTCAGCCGCTACCCCGACCACATGAAGCAGCACGACTTCTTCAAGTCCGCCATGCCCGAAGGCTACGT
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CGACACCCTGGTGAACCGCATCGAGCTGAAGGGCATCGACTTCAAGGAGGACGGCAACATCCTGGGGCA
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GGTGAACTTCAAGATCCGCCACAACATCGAGGACGGCAGCGTGCAGCTCGCCGACCACTACCAGCAGAA
CACCCCCATCGGCGACGGCCCCGTGCTGCTGCCCGACAACCACTACCTGAGCACCCAGTCCGCCCTGAGC
AAAGACCCCAACGAGAAGCGCGATCACATGGTCCTGCTGGAGTTCGTGACCGCCGCCGGGATCACTCTC
GGCATGGACGAGCTGTACAAGTAA-3'

FIG.30C

pLenti-dCas13-ADAR1$_{DD}$

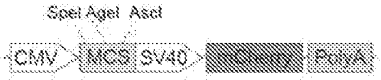


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ACCCCAGGAGGAAAAGAACTTTTATCTCTGCCCAGTATAG-3'(SEQ ID NO:341)

FIG.31

pLenti-MCS-mCherry backbone



5'cgataagcttgggagttccgcgttacataacttacggtaaatggcccgcctggctgaccgcccaacgacccccgcccattgacgtcaataatgac
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agttgtggtttgtccaaactcatcaatgtatcttatcatgtctggctctagctatcccgcccctа-3' (SEQ ID NO:342)

FIG.32

pLenti-arRNA-BFP backbone



5'gagggcctatttcccatgattccttcatatttgcatatacgatacaaggctgttagagagataattagaattaatttgactgtaaaca
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ggaacctcttacgtgccgatcaacgtctcattttcgccaaaagttggcccagggcttcccggtatcaacagggacaccaggatttta
tttattctgcgaagtgatcttccgtcacaggtatttattcggcgcaaagtgcgtcgggtgatgctgccaacttagtcgactacaggtc
actaataccatctaagtagttgattcatagtgactggatatgttgtgttttacagtattatgtagtctgttttttatgcaaaatctaatttaat
atattgatatttatatcattttacgtttctcgttcagctttcttgtacaaagtggttgatctagagggcccgcggttcgaa**cgtctc**ttgat
catatggcgcgcccctcgaggtcgacggtatcgataagctcgcttcacgagattccagcaggtcgagggacctaataacttcgtat
agcatacattatacgaagttatattaagggttccaagcttaagcggccgcgtggataaccgtattaccgccatgcattagttattaat
agtaatcaattacggggtcattagttcatagcccatatatggagttccgcgttacataacttacggtaaatggcccgcctggctgac
cgcccaacgacccccgcccattgacgtcaataatgacgtatgttcccatagtaacgccaatagggactttccattgacgtcaatgg
gtggagtatttacggtaaactgcccacttggcagtacatcaagtgtatcatatgccaagtacgccccctattgacgtcaatgacggt
aaatggcccgcctggcattatgcccagtacatgaccttatgggactttcctacttggcagtacatctacgtattagtcatcgctattac
catggtgatgcggttttggcagtacatcaatgggcgtggatagcggtttgactcacggggatttccaagtctccaccccattgacg
tcaatgggagtttgttttggcaccaaaatcaacgggactttccaaaatgtcgtaacaactccgccccattgacgcaaatgggcggt
aggcgtgtacggtgggaggtctatataagcagagctggtttagtgaaccgtcagatccgctagcgccacc**atgagcgagctga**
ttaaggagaacatgcacatgaagctgtacatggagggcaccgtggacaaccatcacttcaagtgcacatccgagggcg
aaggcaagccctacgagggcacccagaccatgagaatcaaggtggtcgagggcggccctctcccctttcgccttcgacat
cctggctactagcttcctctacggcagcaagaccttcatcaaccacacccagggcatccccgactttttcaagcagtccttt
ccctgagggcttcacatgggagagagtcaccacatacgaagacggggggcgtgctgaccgctaccccaggacaccagcct
ccaggacggctgcctcatctacaacgtcaagatcagaggggtgaacttcacatccaacggccctgtgatgcagaagaa
aacactcggctgggaggccttcaccgagactctgtaccccgctgacggcggcctggaaggcagaaacgacatggccct
gaagctcgtgggcgggagccatctgatgcaaacatcaagaccacatatagatccaagaaacccgctaagaacctcaa
gatgcctggcgtctactatgtggactacagactggaaagaatcaaggaggccaacaacgagacctacgtcgagcagca
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FIG.33

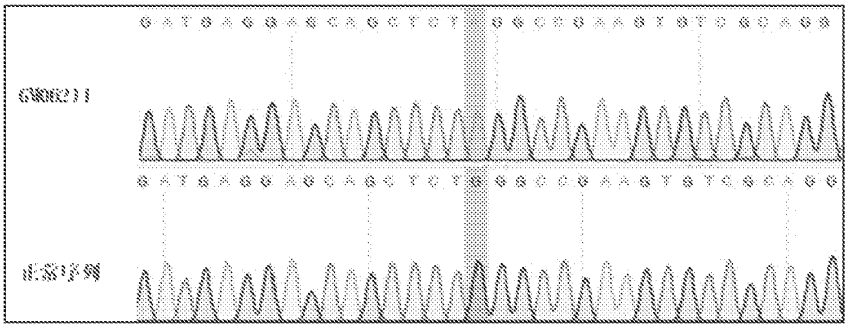


FIG. 34

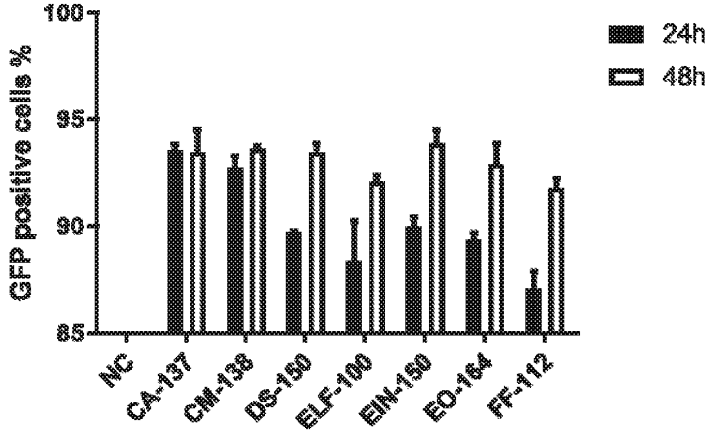

100
95
90
85
GFP positive cells %
24h
48h
NC
CA-137
CM-138
DS-150
ELF-100
EIN-150
EO-164
FF-112

FIG. 35

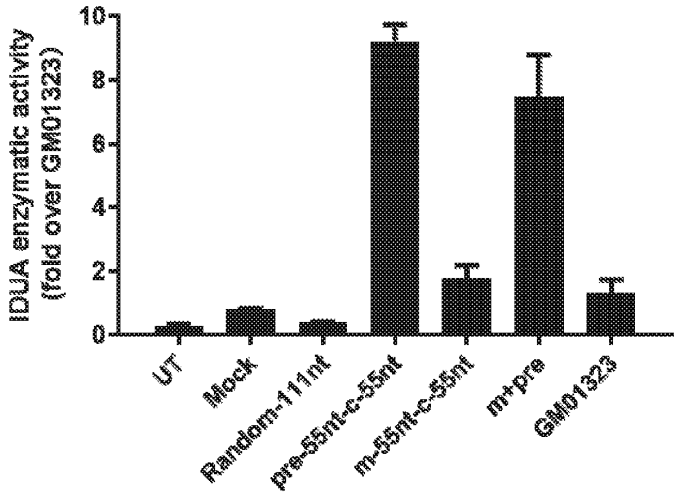


FIG. 36A

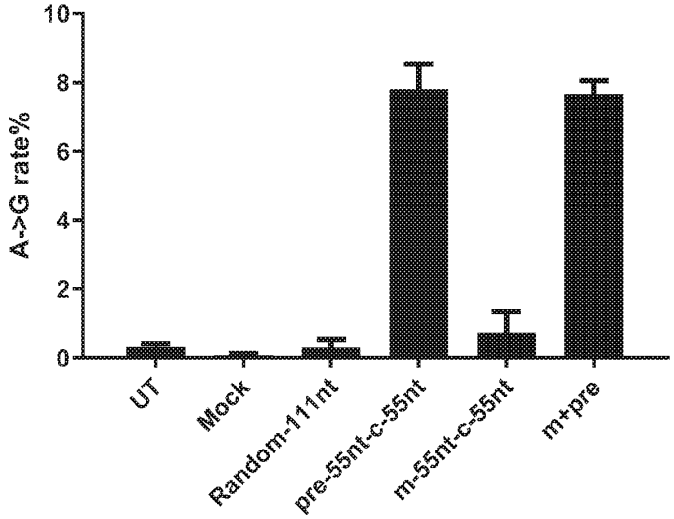


FIG. 36B

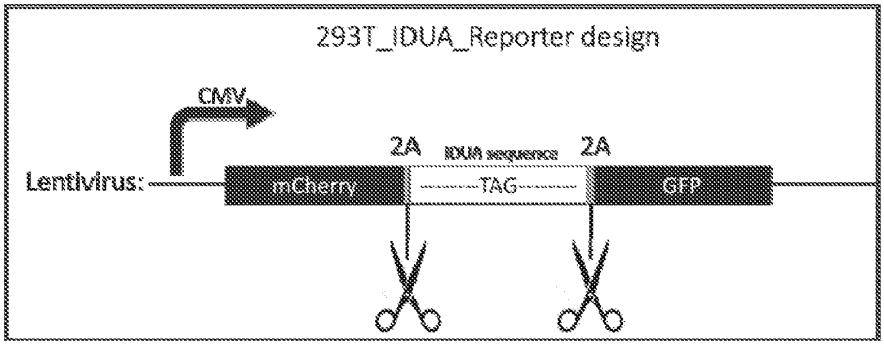


FIG. 37A

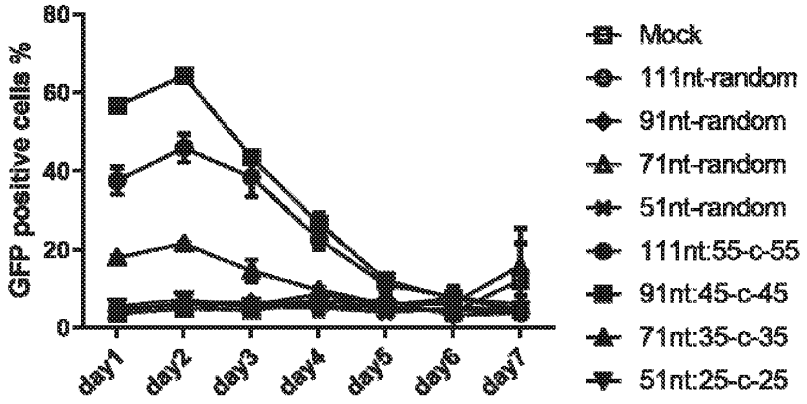


FIG. 37B

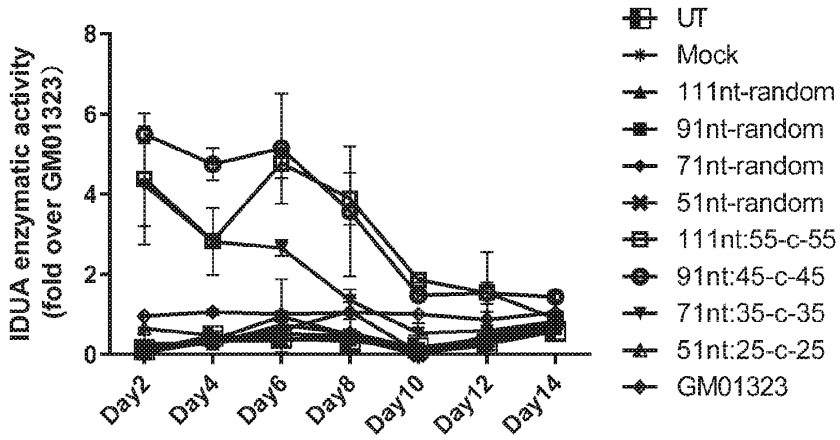


FIG. 38A

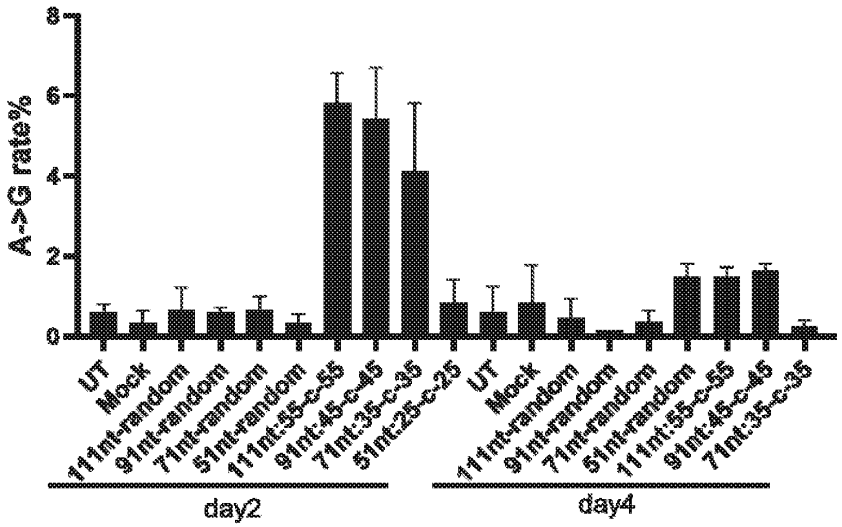


FIG. 38B

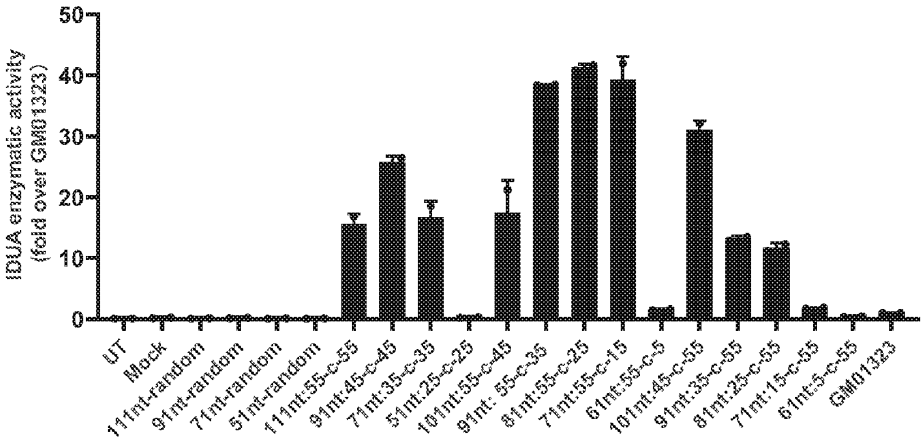


FIG. 39A

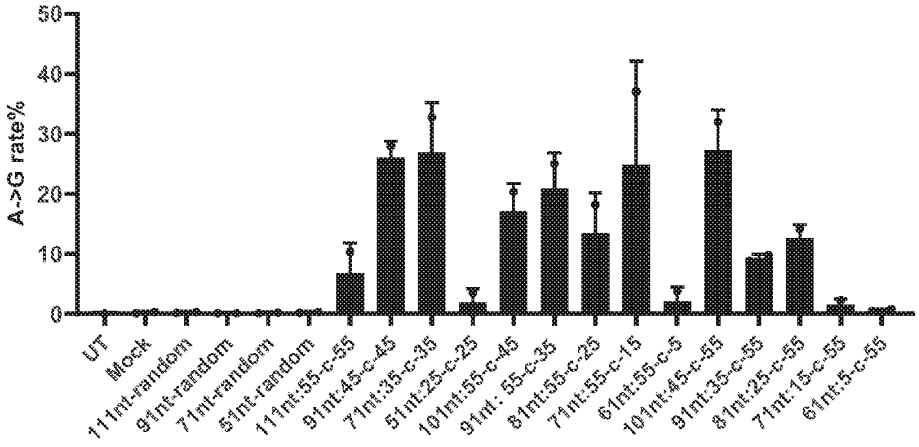


FIG. 39B

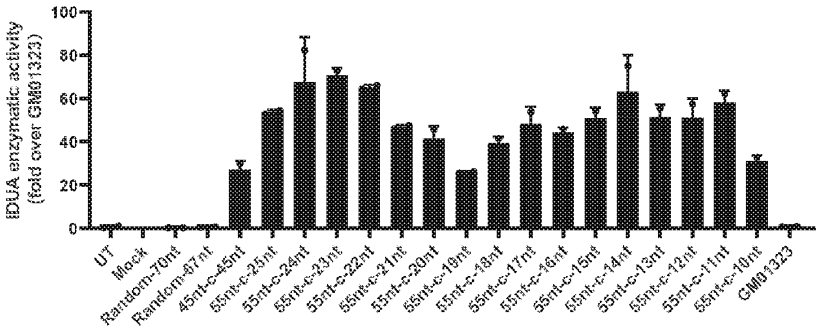


FIG. 40A

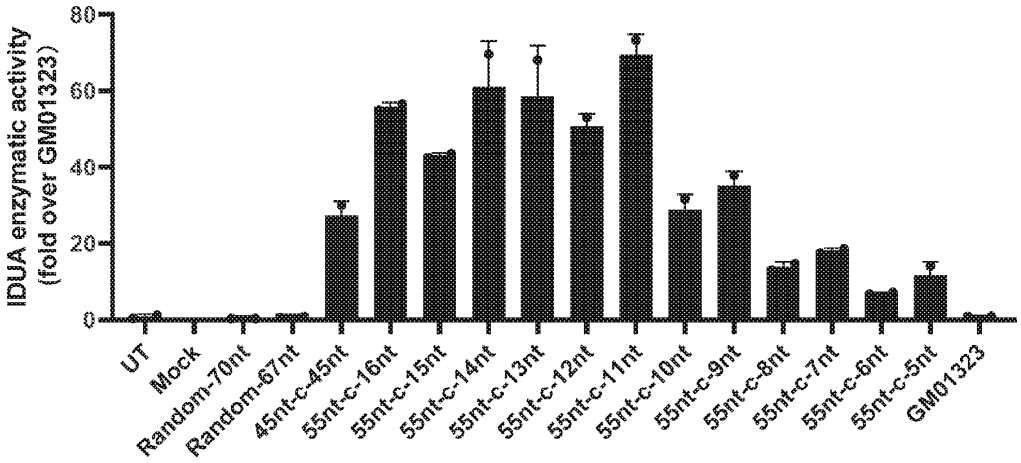


FIG. 40B

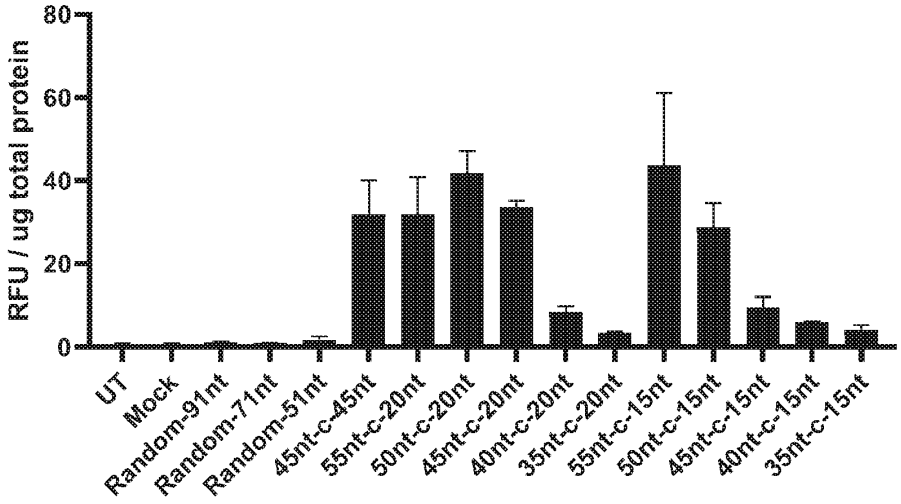

RFU / ug total protein
80
60
40
20
0
UT
Mock
Random-91nt
Random-71nt
Random-51nt
45nt-c-45nt
55nt-c-20nt
50nt-c-20nt
45nt-c-20nt
40nt-c-20nt
35nt-c-20nt
55nt-c-15nt
50nt-c-15nt
45nt-c-15nt
40nt-c-15nt
35nt-c-15nt

FIG. 41

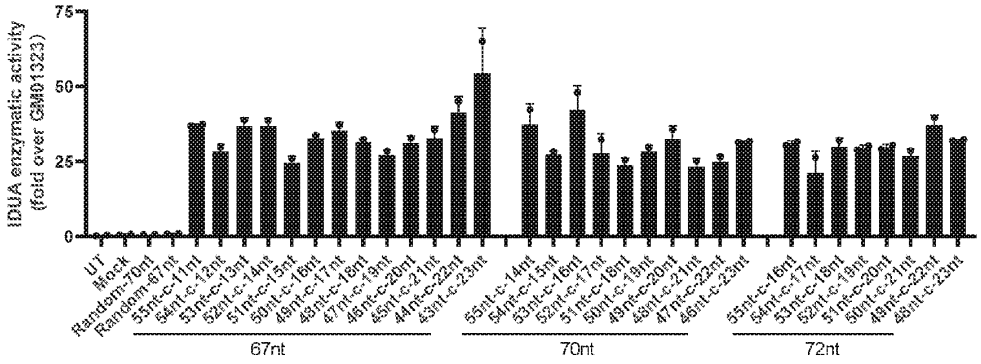

IDUA enzymatic activity
(fold over GM01323)
75
50
25
0
UT
Mock
Random-70nt
Random-67nt
55nt-c-11nt
54nt-c-12nt
53nt-c-13nt
52nt-c-14nt
51nt-c-15nt
50nt-c-16nt
49nt-c-17nt
48nt-c-18nt
47nt-c-19nt
46nt-c-20nt
45nt-c-21nt
44nt-c-22nt
43nt-c-23nt
55nt-c-14nt
54nt-c-15nt
53nt-c-16nt
52nt-c-17nt
51nt-c-18nt
50nt-c-19nt
49nt-c-20nt
48nt-c-21nt
47nt-c-22nt
46nt-c-23nt
55nt-c-16nt
54nt-c-17nt
53nt-c-18nt
52nt-c-19nt
51nt-c-20nt
50nt-c-21nt
49nt-c-22nt
48nt-c-23nt
67nt
70nt
72nt

FIG. 42

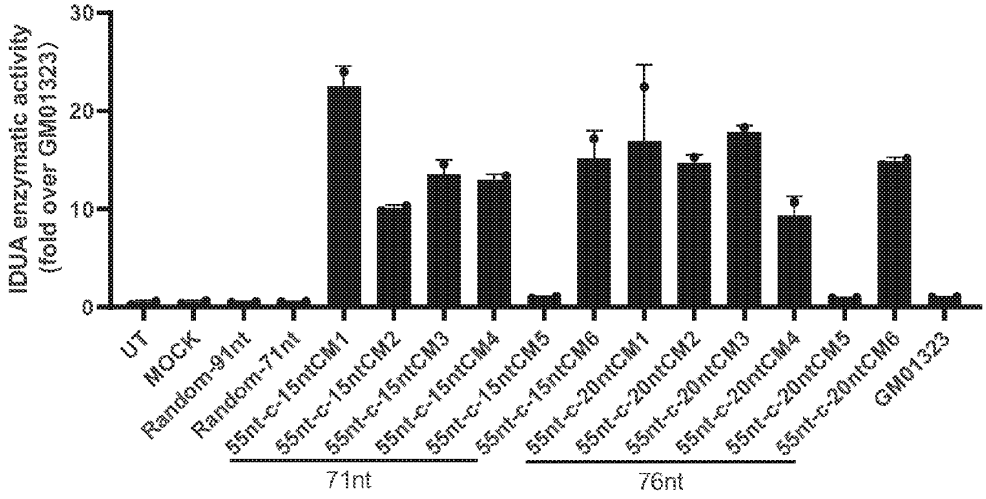

IDUA enzymatic activity
(fold over GM01323)
30
20
10
0
UT
MOCK
Random-91nt
Random-71nt
55nt-c-15ntCM1
55nt-c-15ntCM2
55nt-c-15ntCM3
55nt-c-15ntCM4
55nt-c-15ntCM5
55nt-c-15ntCM6
55nt-c-20ntCM1
55nt-c-20ntCM2
55nt-c-20ntCM3
55nt-c-20ntCM4
55nt-c-20ntCM5
55nt-c-20ntCM6
GM01323
71nt
76nt

图 43A

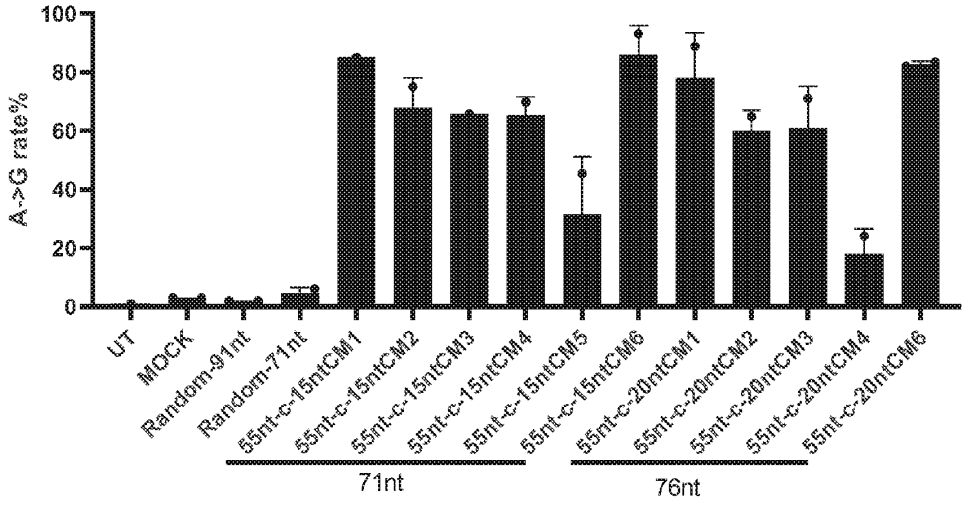

A->G rate%
100
80
60
40
20
0
UT
MOCK
Random-91nt
Random-71nt
55nt-c-15ntCM1
55nt-c-15ntCM2
55nt-c-15ntCM3
55nt-c-15ntCM4
55nt-c-15ntCM5
55nt-c-15ntCM6
55nt-c-20ntCM1
55nt-c-20ntCM2
55nt-c-20ntCM3
55nt-c-20ntCM4
55nt-c-20ntCM6
71nt
76nt

图 43B

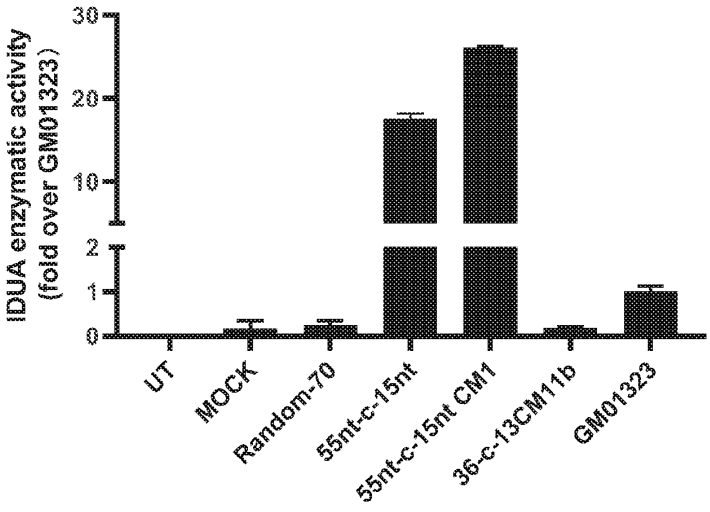


FIG. 44

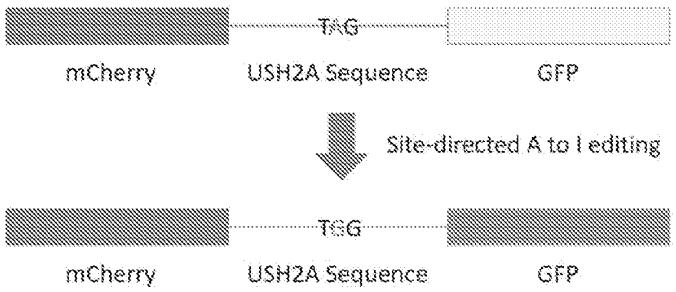


FIG. 45A

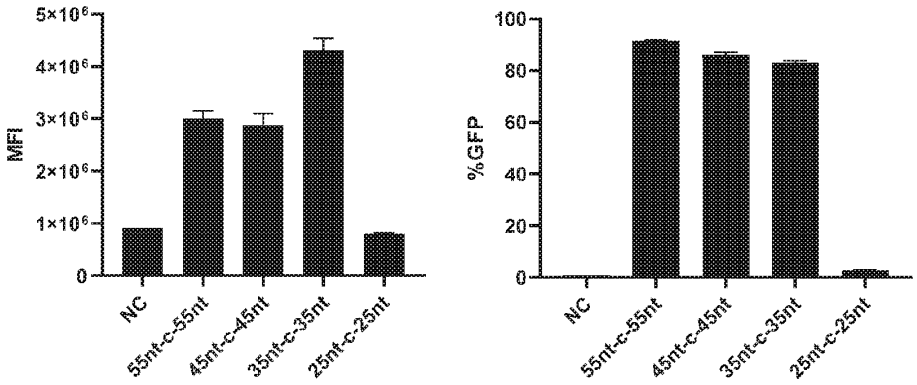


FIG. 45B

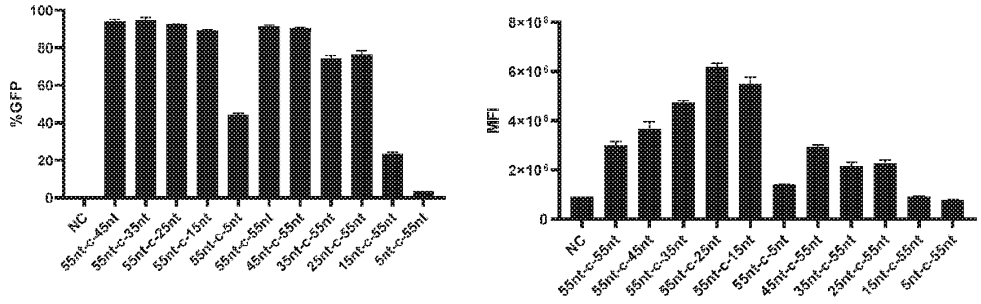


FIG. 45C

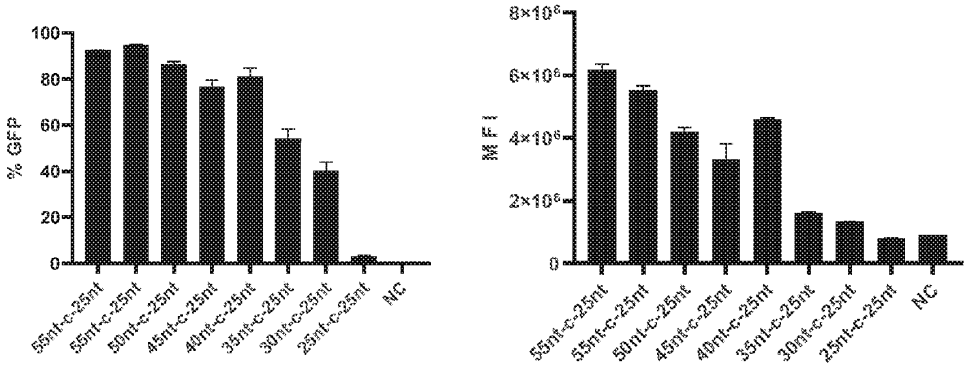

% GFP
100
80
60
40
20
0
55nt-c-25nt
55nt-c-25nt
50nt-c-25nt
45nt-c-25nt
40nt-c-25nt
35nt-c-25nt
30nt-c-25nt
25nt-c-25nt
NC
MFI
8×10⁶
6×10⁶
4×10⁶
2×10⁶
0
55nt-c-25nt
55nt-c-25nt
50nt-c-25nt
45nt-c-25nt
40nt-c-25nt
35nt-c-25nt
30nt-c-25nt
25nt-c-25nt
NC

FIG. 45D