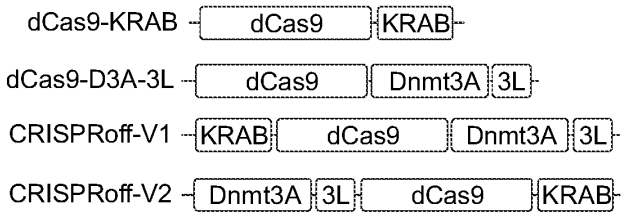

FIG. 1A

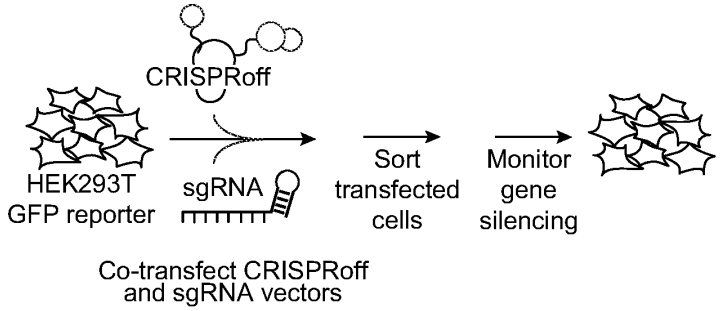

FIG. 1B

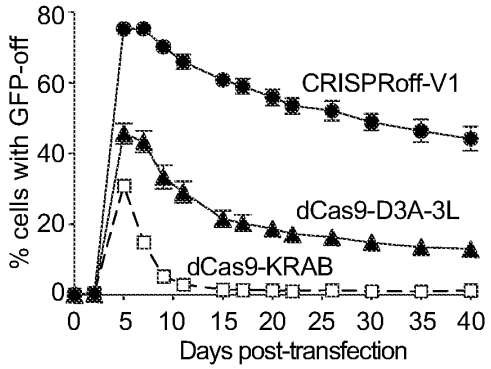

FIG. 1C

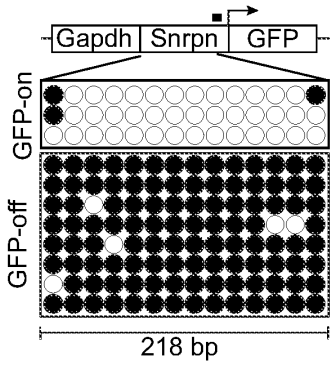

FIG. 1D

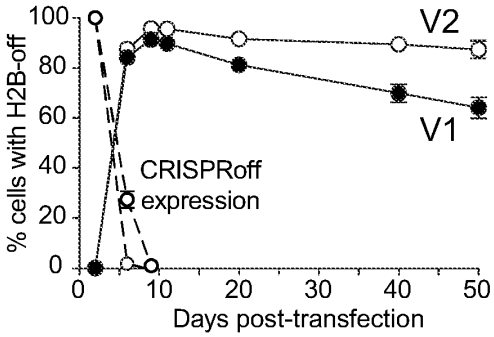

FIG. 1E

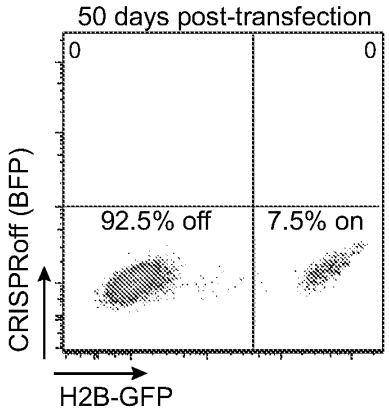

FIG. 1F

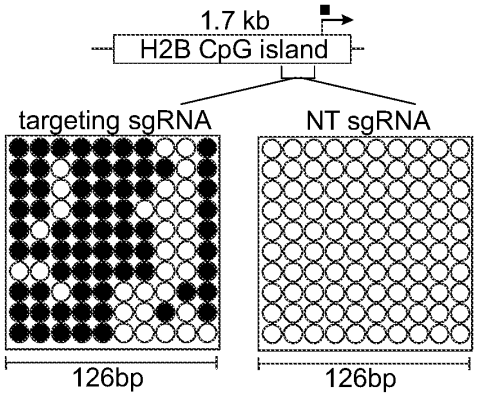

FIG. 1G

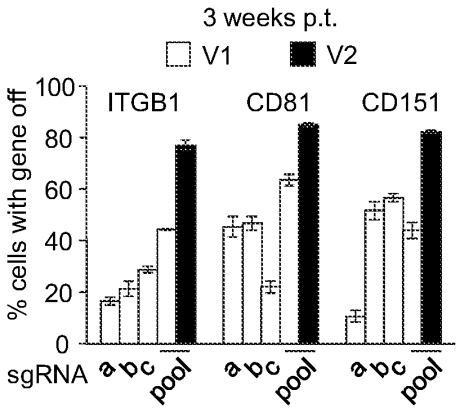

FIG. 1H

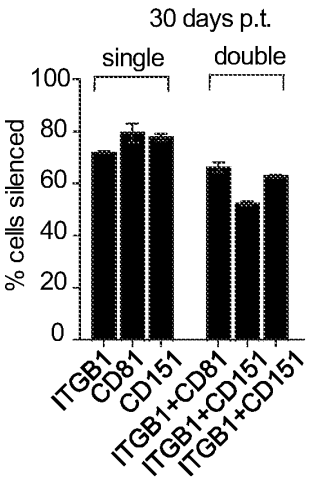

FIG. 1I

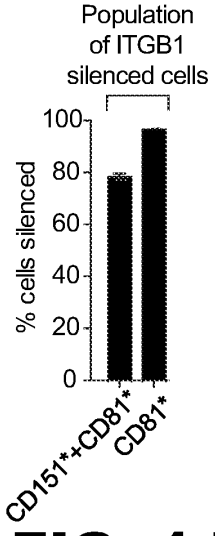

FIG. 1J

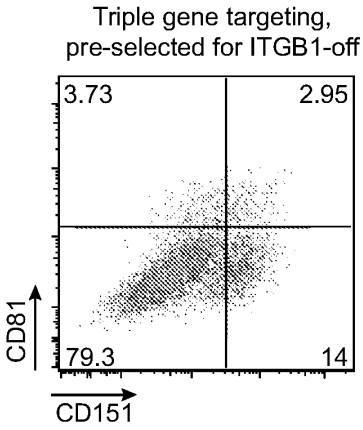
Triple gene targeting,
pre-selected for ITGB1-off
3.73
2.95
79.3
14
CD81
CD151

FIG. 1K

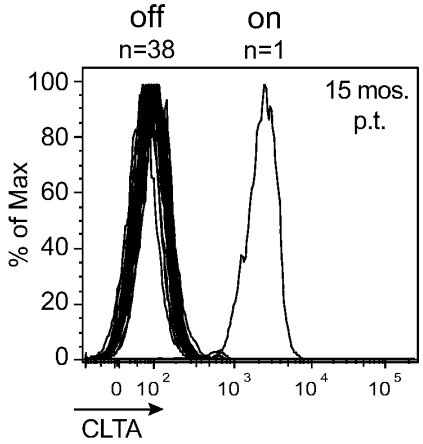
off
n=38
on
n=1
15 mos.
p.t.
% of Max
100
80
60
40
20
0
0 10^2
10^3
10^4
10^5
CLTA

FIG. 1L

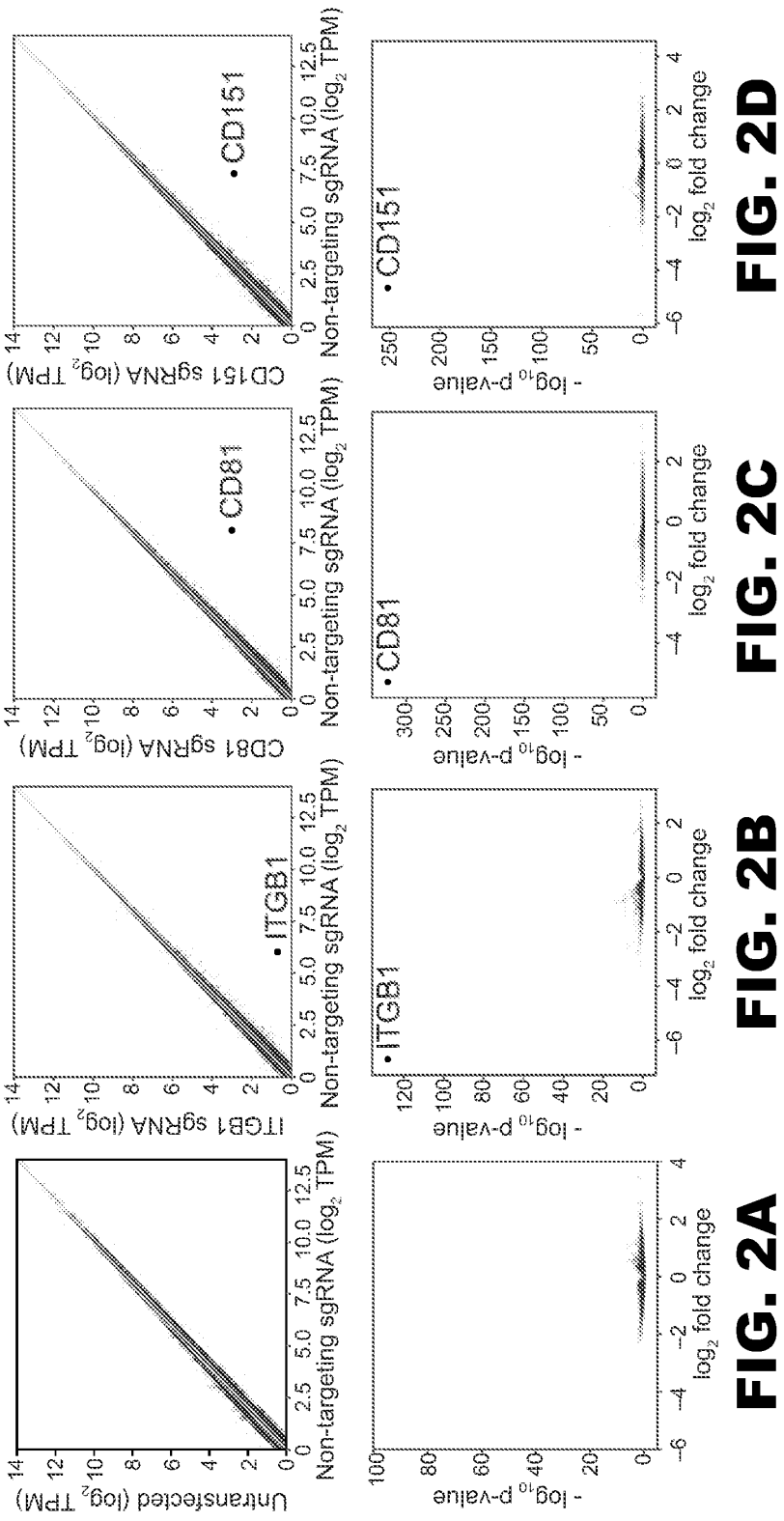

FIG. 2A

FIG. 2B

FIG. 2C

FIG. 2D

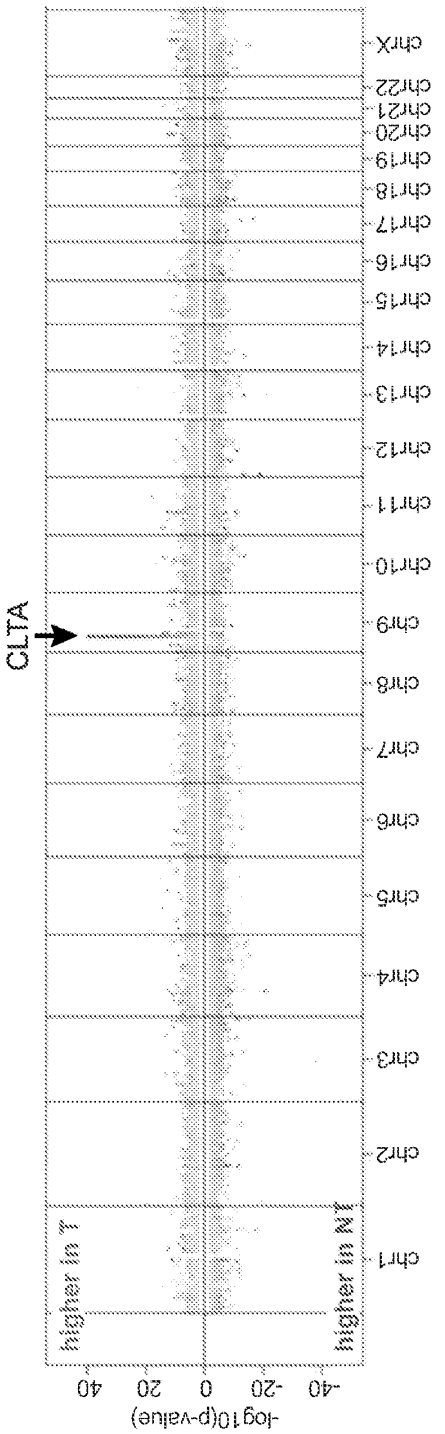
higher in T
higher in NT
-log10(p-value)
-40
-20
0
20
40
CLTA
chr1
chr2
chr3
chr4
chr5
chr6
chr7
chr8
chr9
chr10
chr11
chr12
chr13
chr14
chr15
chr16
chr17
chr18
chr19
chr20
chr21
chr22
chrX

FIG. 2E

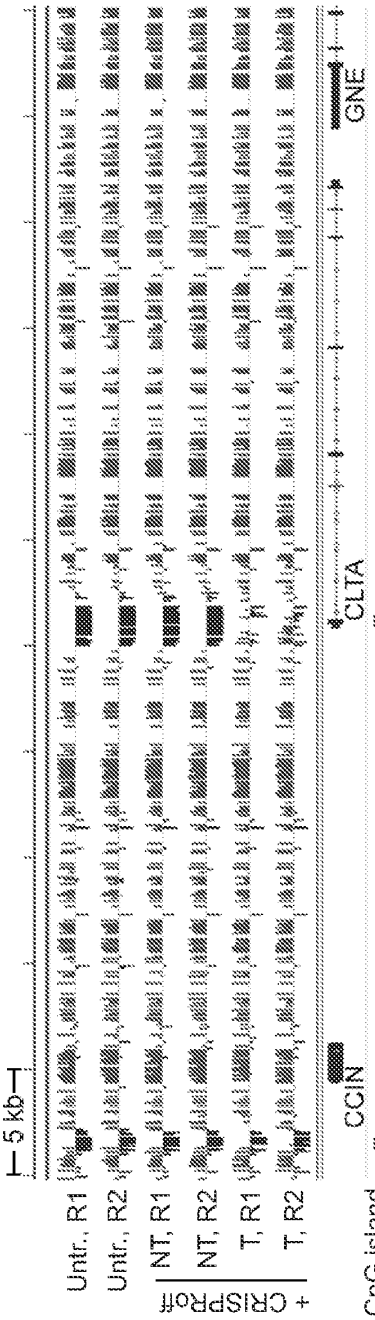
5 kb
Untr., R1
Untr., R2
+ CRISPRoff
NT, R1
NT, R2
T, R1
T, R2
[0-1]
CpG island
CCIN
CLTA
GNE

FIG. 2F

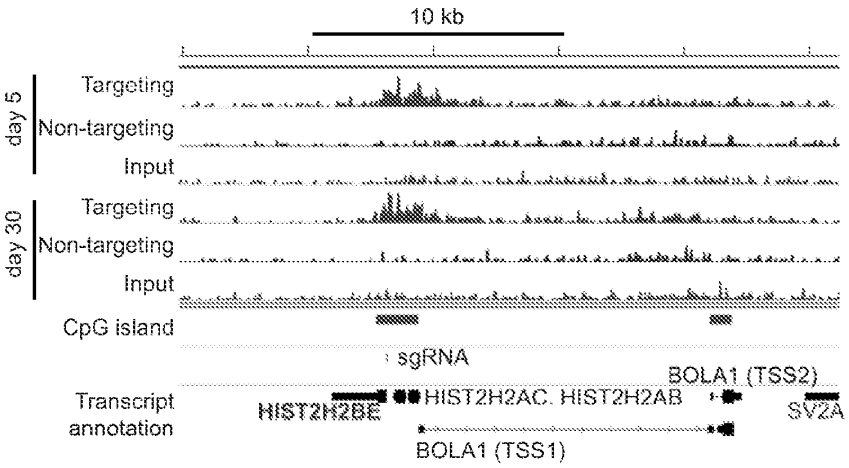
10 kb
day 5
Targeting
Non-targeting
Input
day 30
Targeting
Non-targeting
Input
CpG island
sgRNA
Transcript annotation
HIST2H2BE
HIST2H2AC, HIST2H2AB
BOLA1 (TSS2)
SV2A
BOLA1 (TSS1)

FIG. 2G

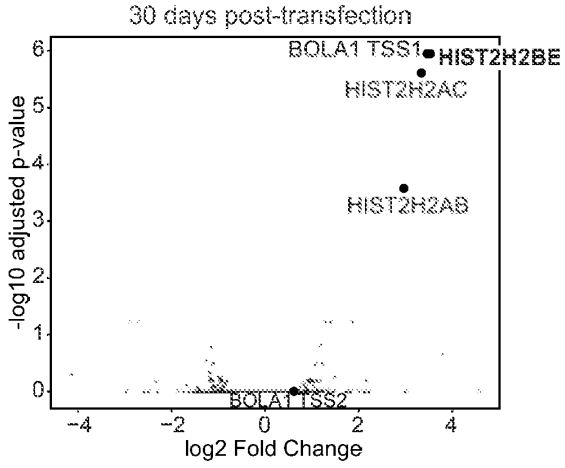
30 days post-transfection
BOLA1 TSS1
HIST2H2BE
HIST2H2AC
HIST2H2AB
BOLA1 TSS2
-log10 adjusted p-value
log2 Fold Change
0
1
2
3
4
5
6
−4
−2
0
2
4

FIG. 2H

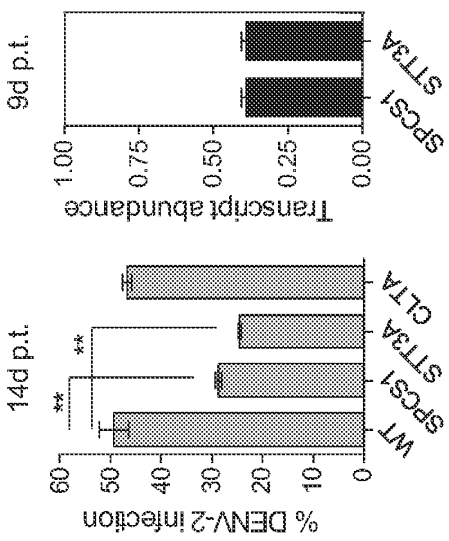

FIG. 3D

FIG. 3C

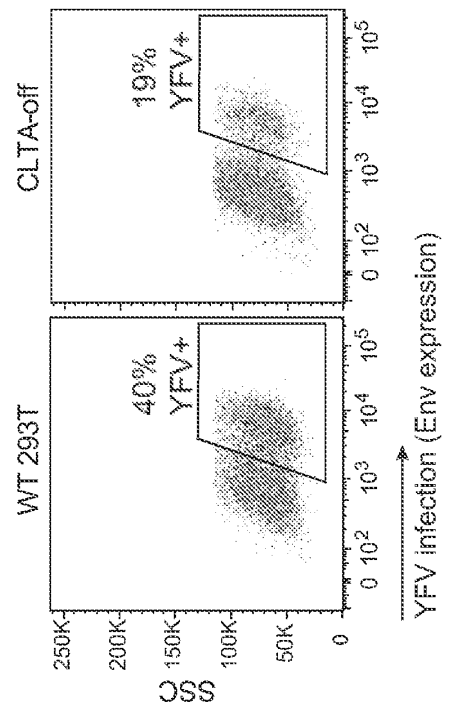

FIG. 3B

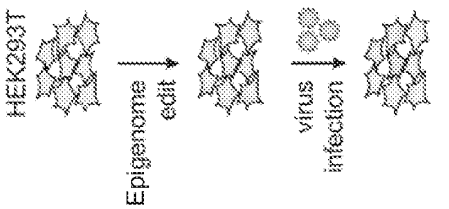

FIG. 3A

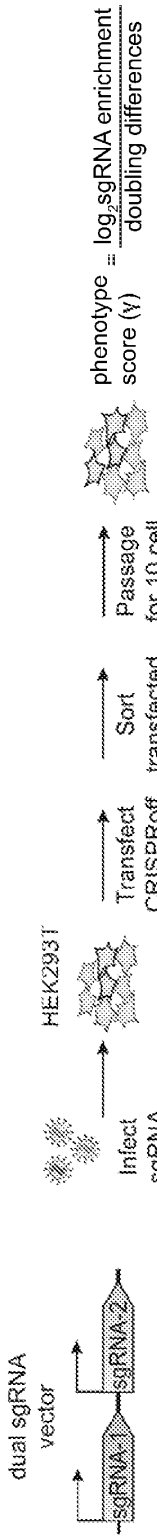

FIG. 4A

FIG. 4B

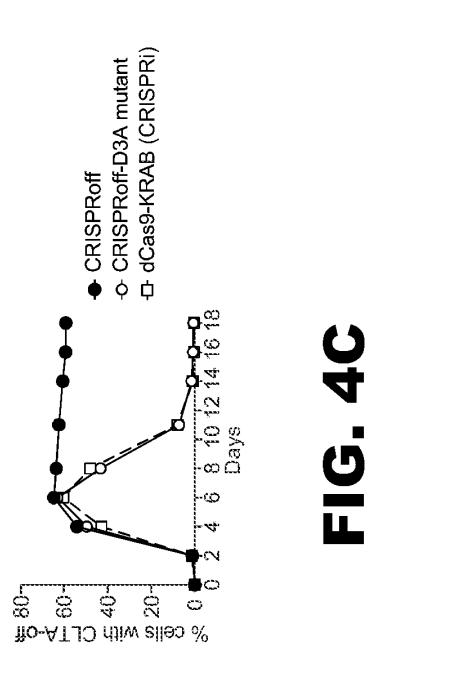

FIG. 4C

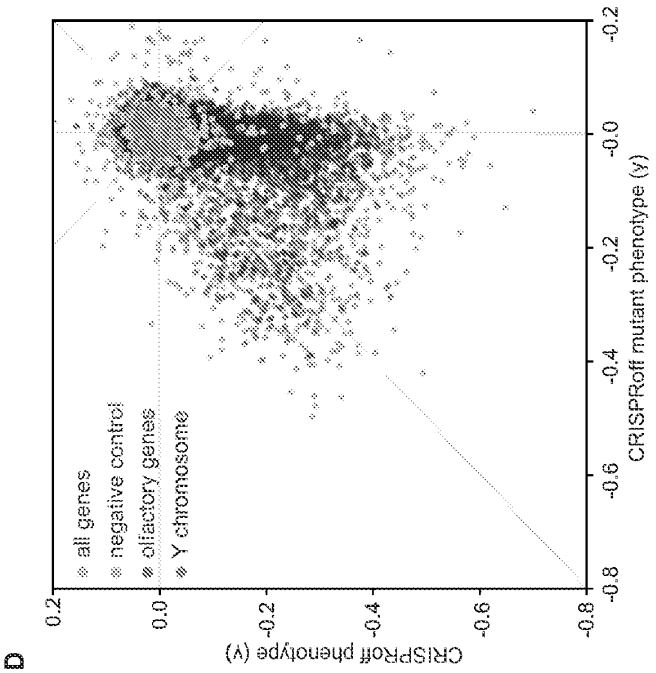

FIG. 4D

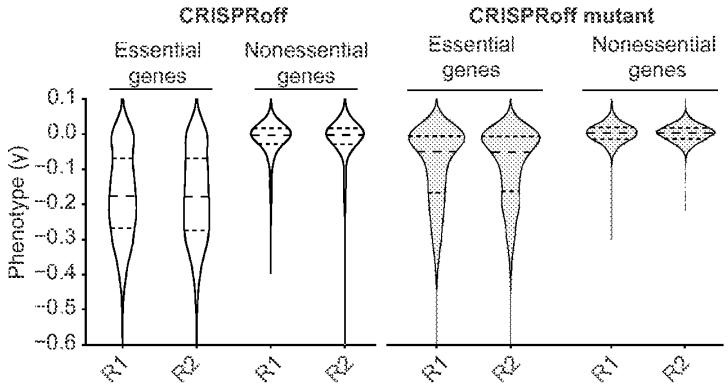

FIG. 4E

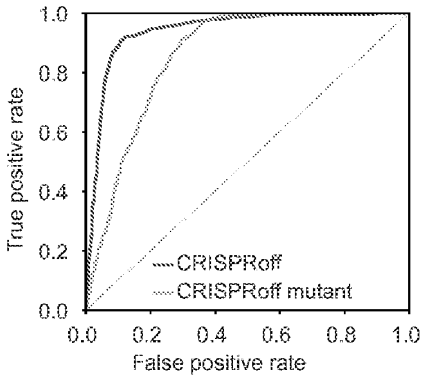

FIG. 4F

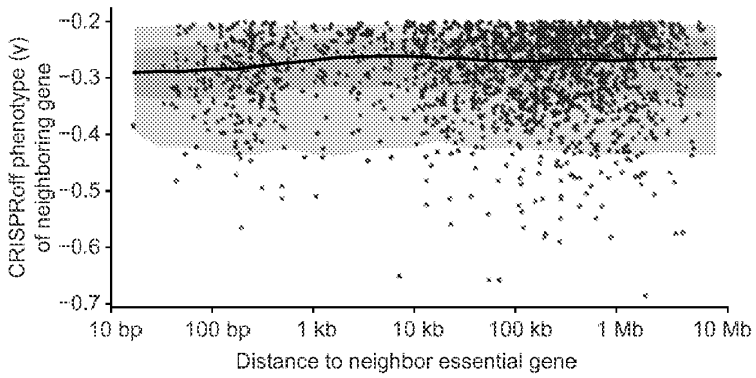

FIG. 4G

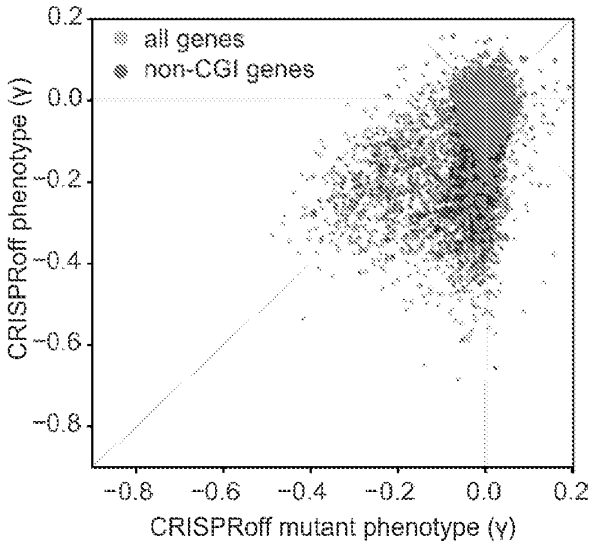

FIG. 5A

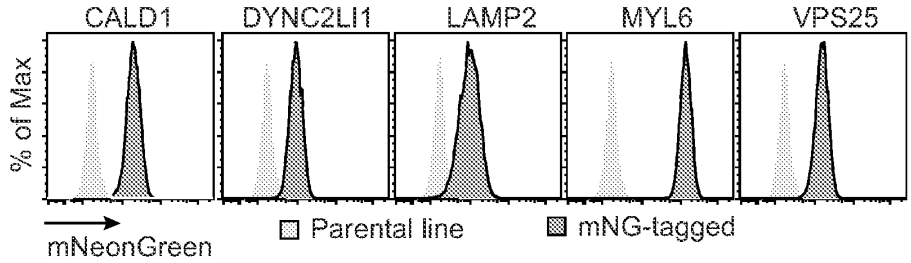

FIG. 5B

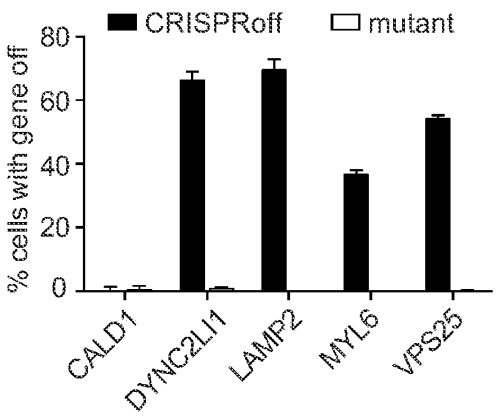

FIG. 5C

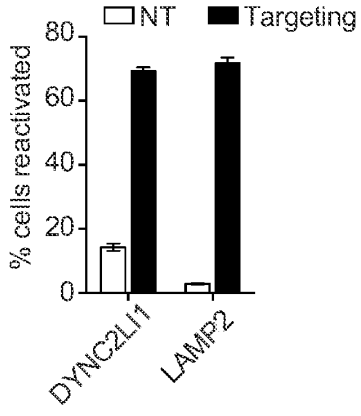

FIG. 5D

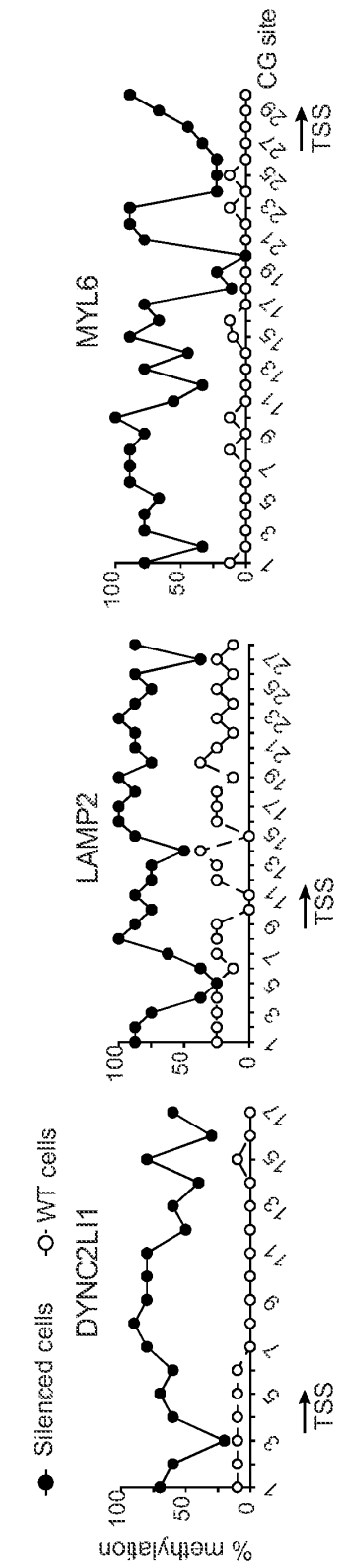

FIG. 5E

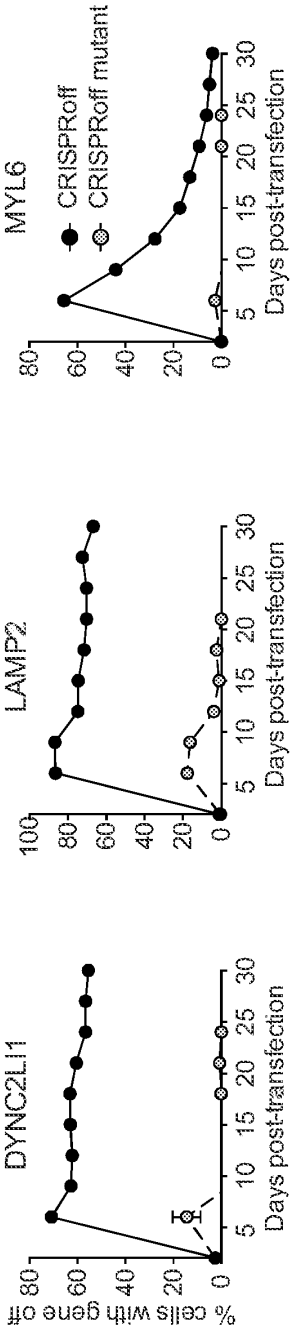

FIG. 5F

FIG. 5G

FIG. 5H

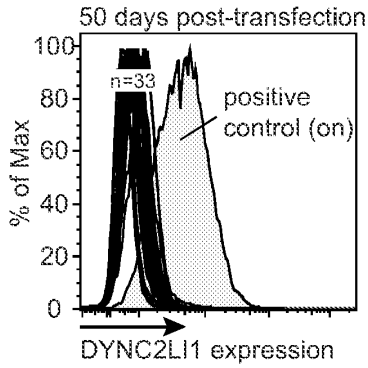

FIG. 5I

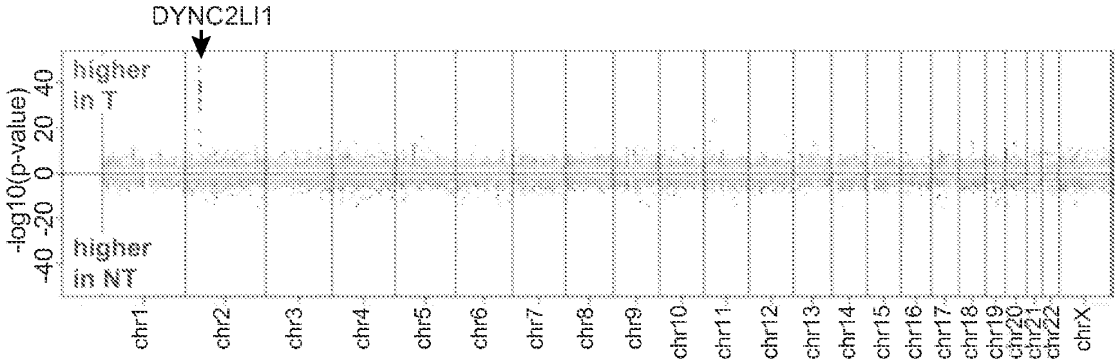

FIG. 5J

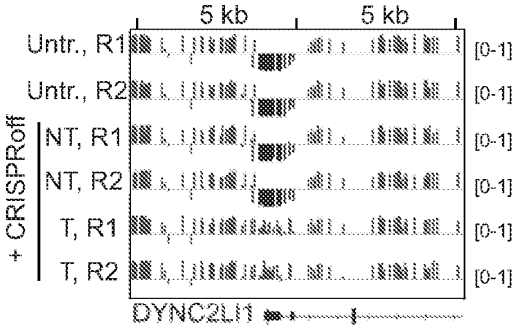

FIG. 5K

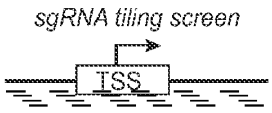

FIG. 6A

# guides	116,085
# NT guides	3,790
Total genes	520
One CGI	425
Multiple CGI	56
No CGI	39

FIG. 6B

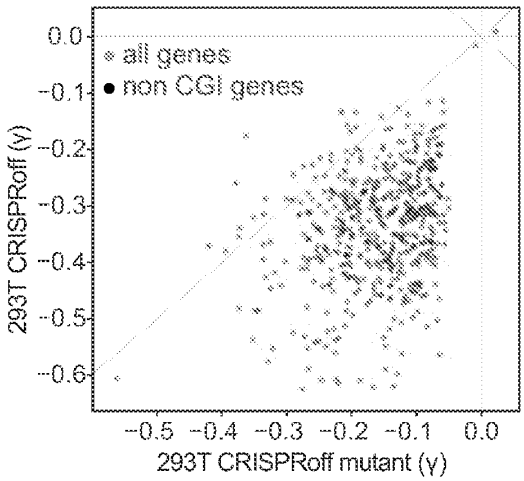

FIG. 6C

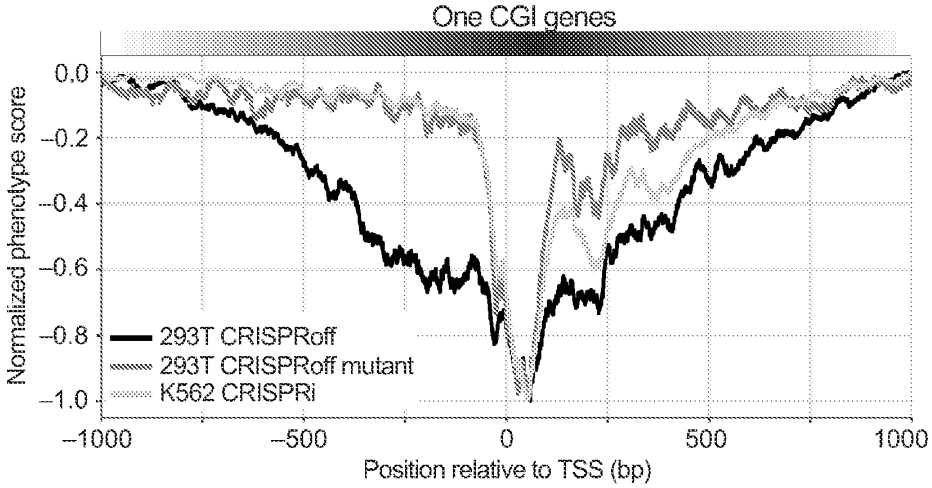

FIG. 6D

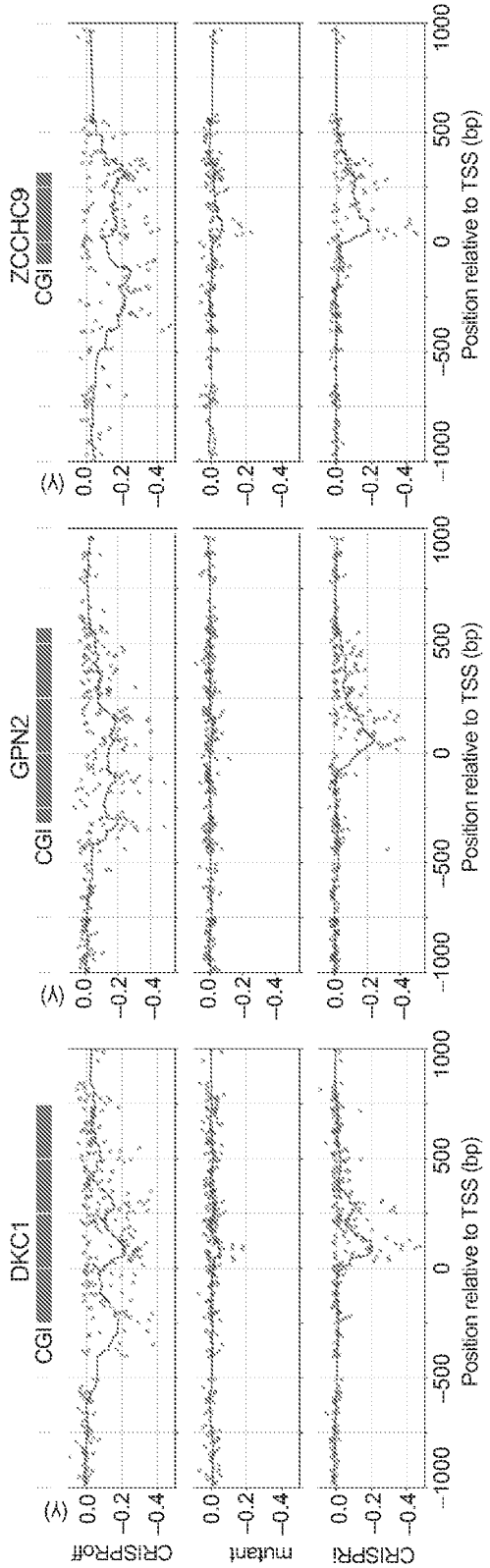

FIG. 6E

FIG. 6F

FIG. 6G

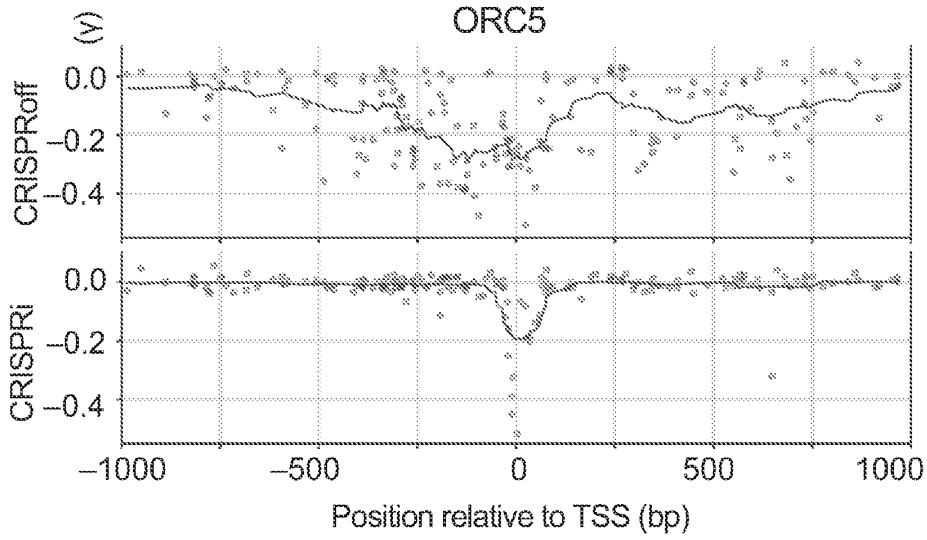
ORC5
(Y)
CRISPRoff
0.0
−0.2
−0.4
CRISPRi
0.0
−0.2
−0.4
−1000
−500
0
500
1000
Position relative to TSS (bp)

FIG. 6H

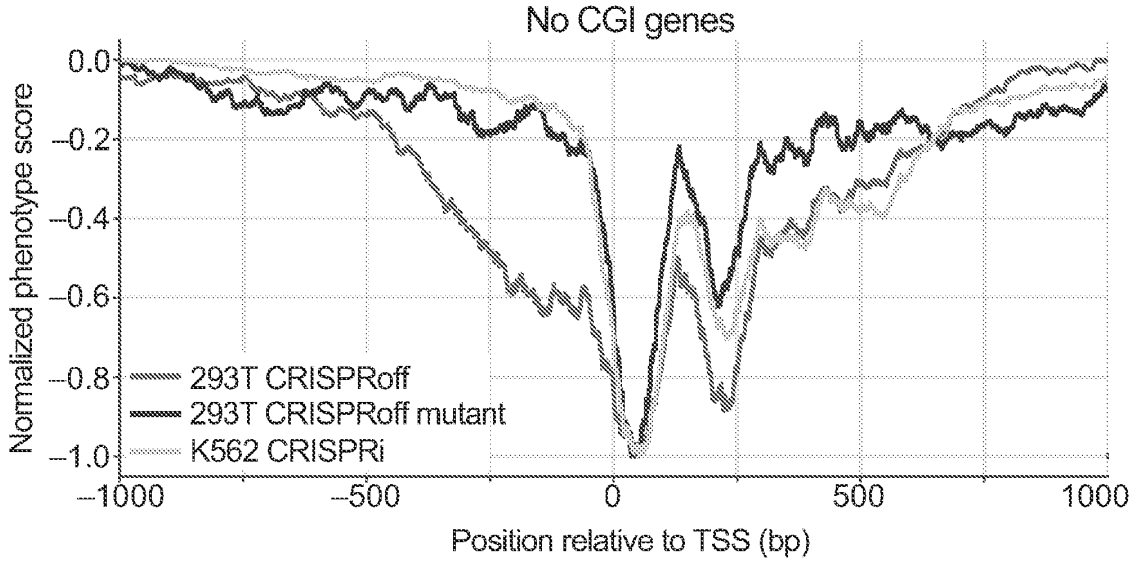
No CGI genes
Normalized phenotype score
0.0
−0.2
−0.4
−0.6
−0.8
−1.0
293T CRISPRoff
293T CRISPRoff mutant
K562 CRISPRi
−1000
−500
0
500
1000
Position relative to TSS (bp)

FIG. 6I

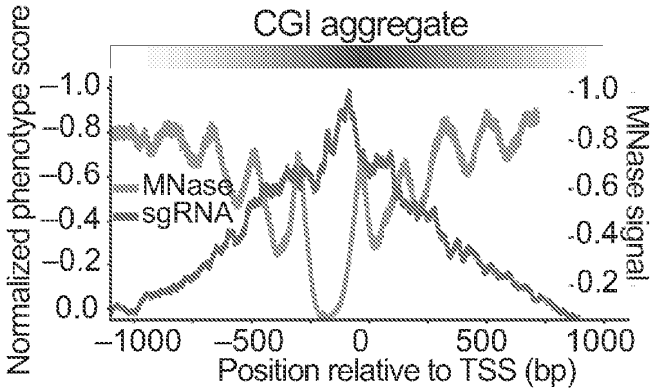

FIG. 6J

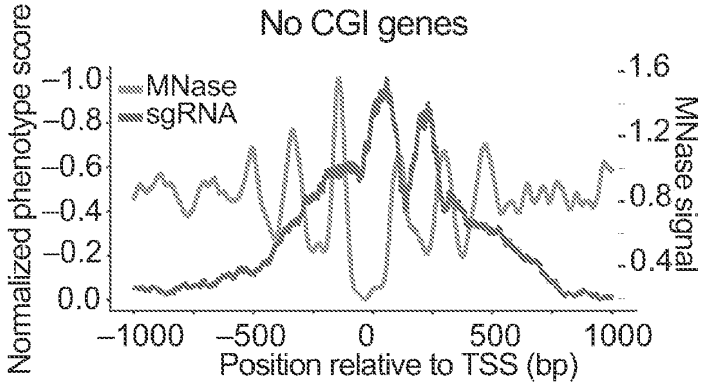

FIG. 6K

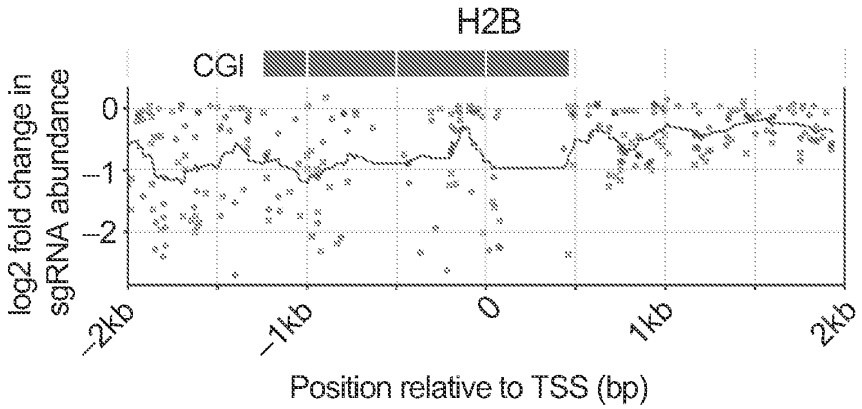

FIG. 6L

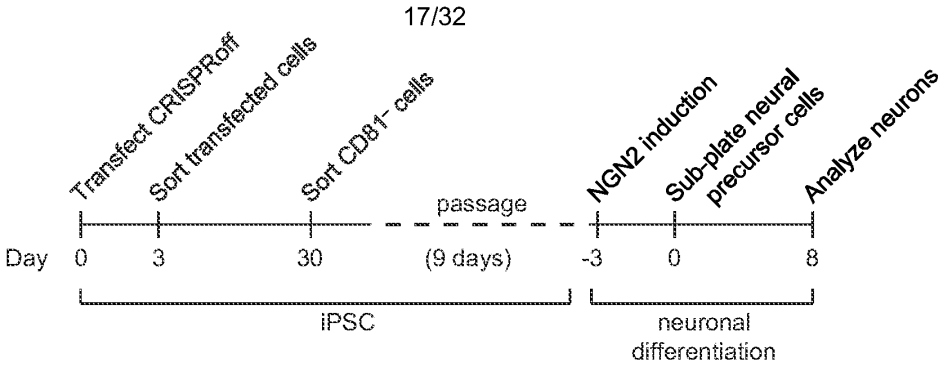

FIG. 7A

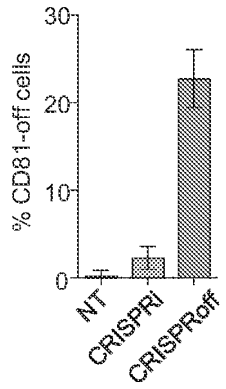

FIG. 7B

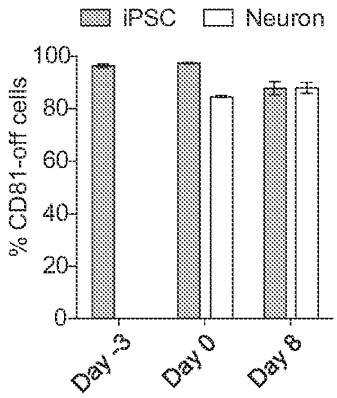

FIG. 7C

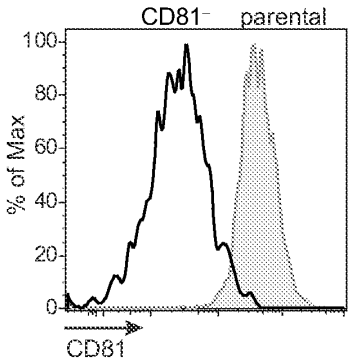

FIG. 7D

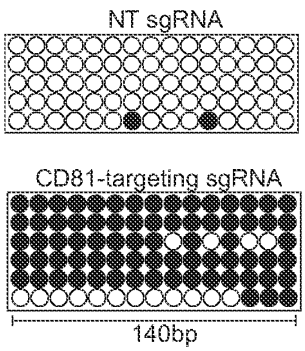

FIG. 7E

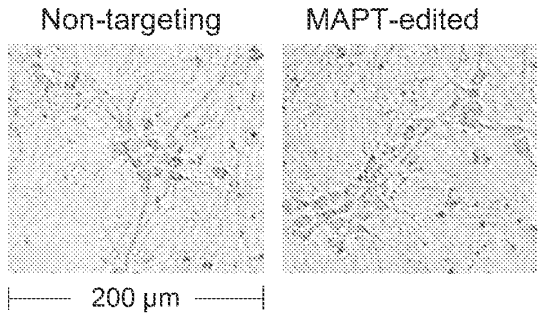

FIG. 7F

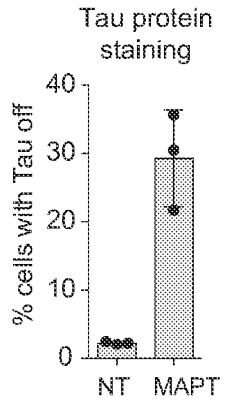

FIG. 7G

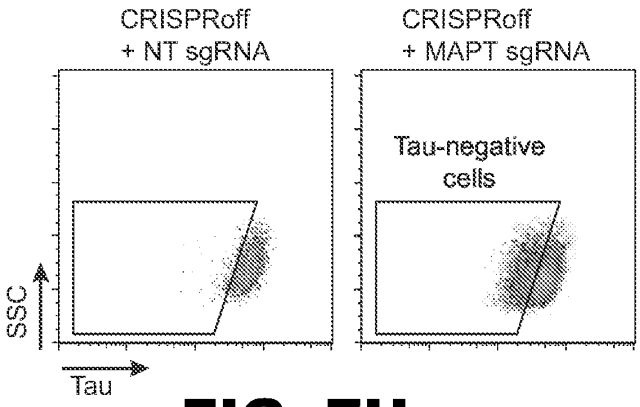

FIG. 7H

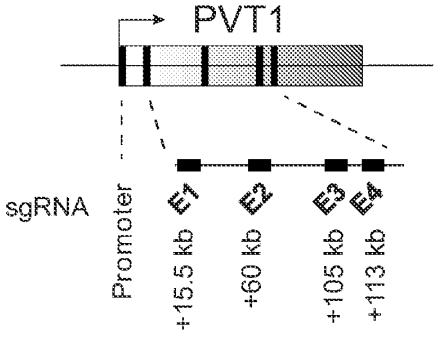

FIG. 7I

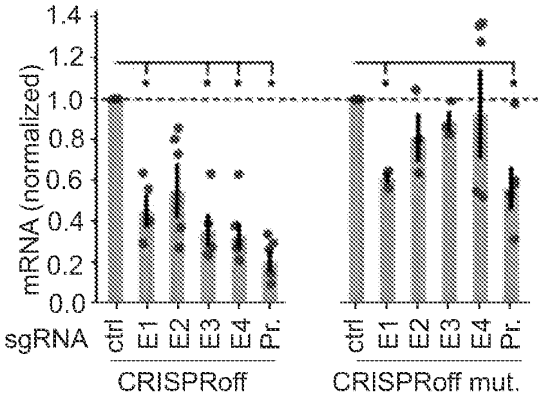

FIG. 7J

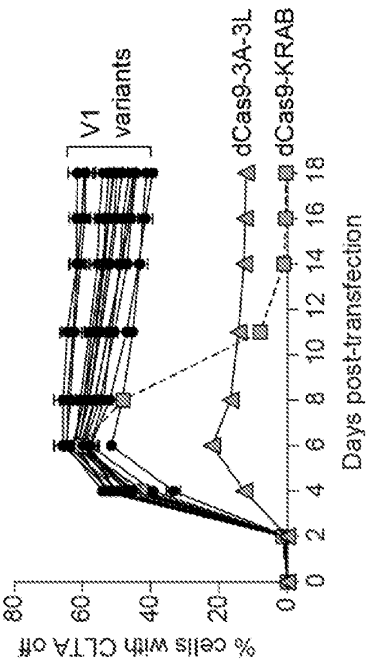

FIG. 8B

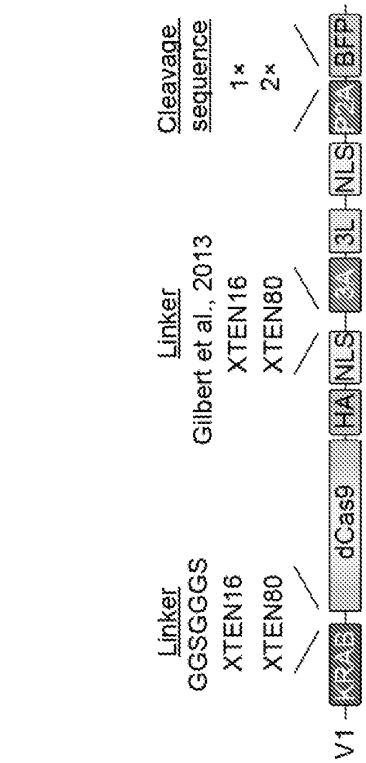

FIG. 8A

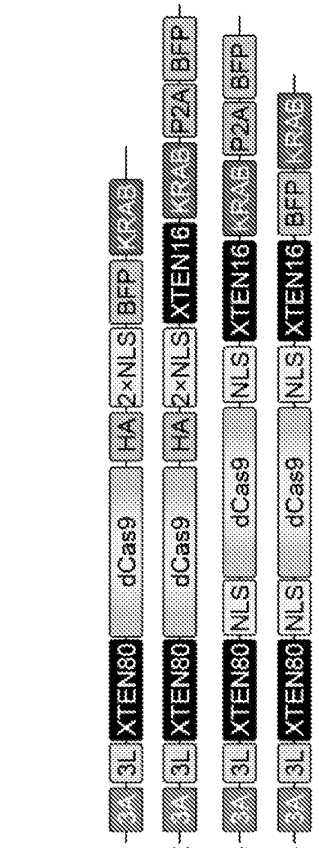

FIG. 8D

FIG. 8C

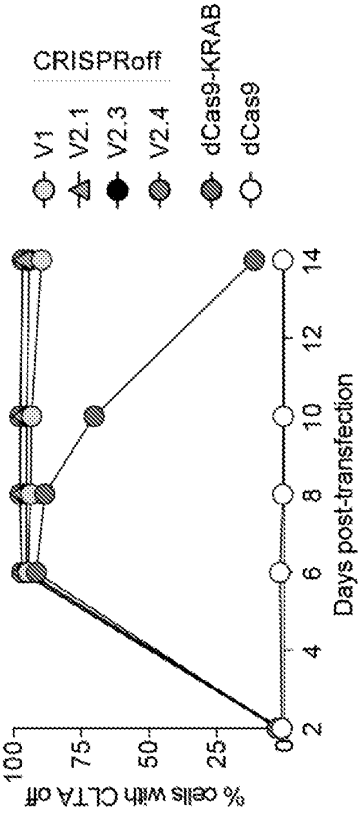

FIG. 8F

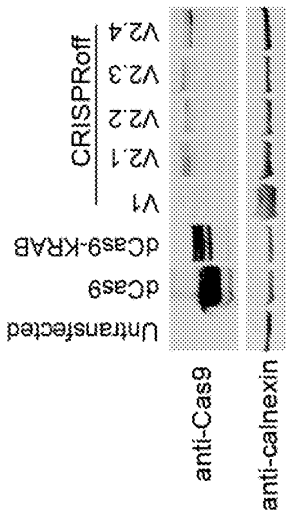

FIG. 8E

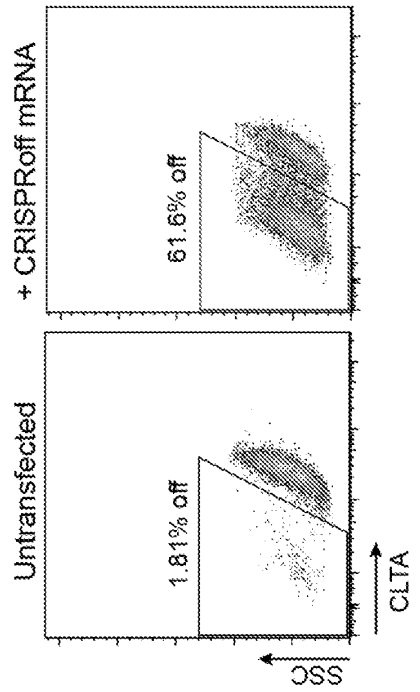

FIG. 8H

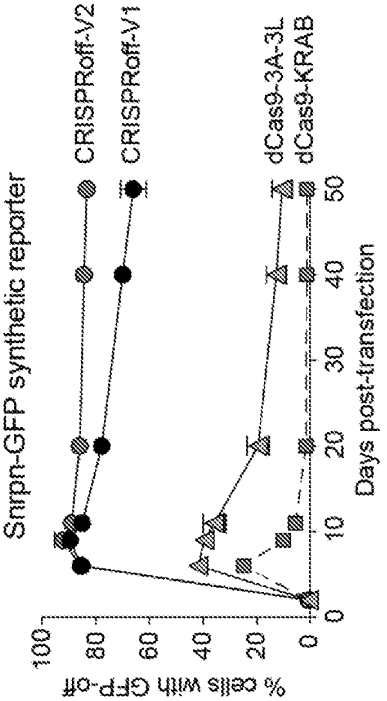

FIG. 8G

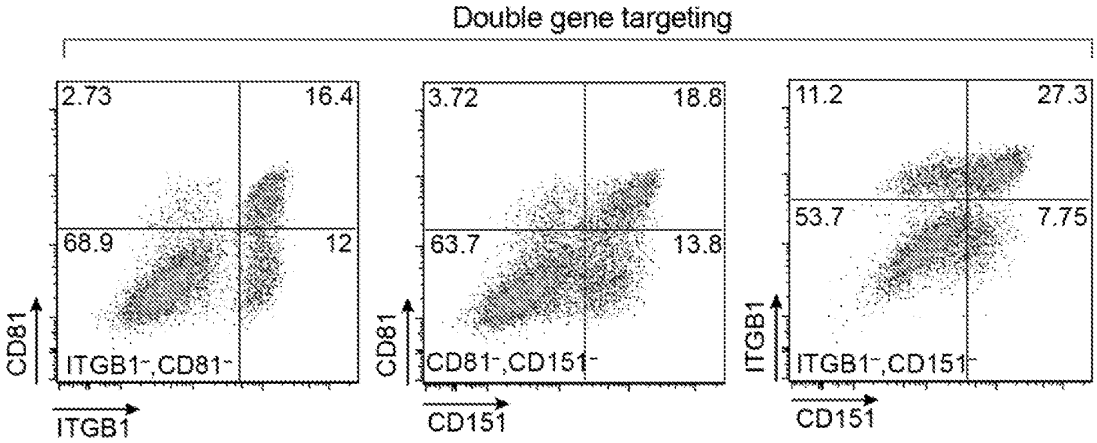

FIG. 8I

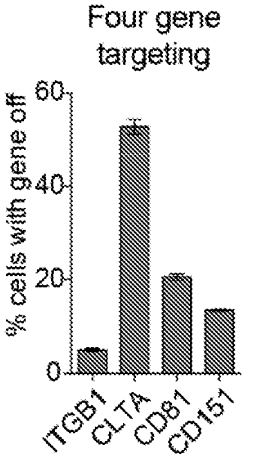

FIG. 8J

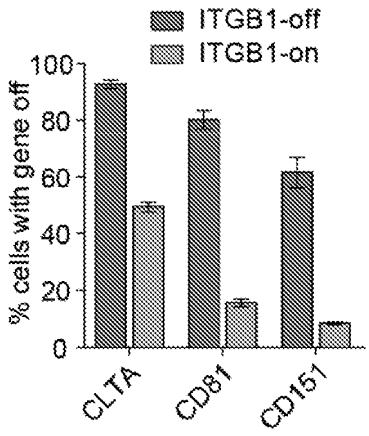

FIG. 8K

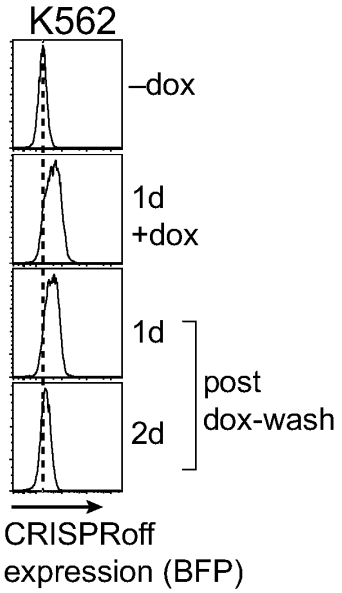

FIG. 9A

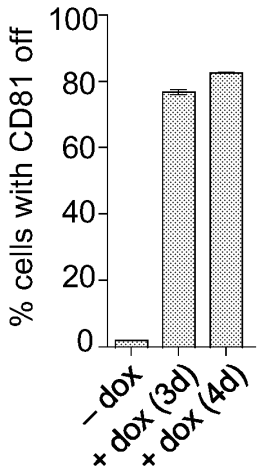

FIG. 9B

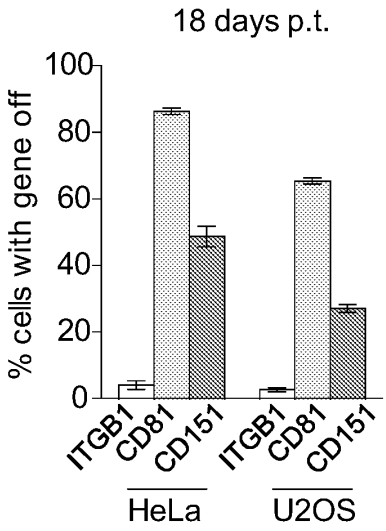

FIG. 9C

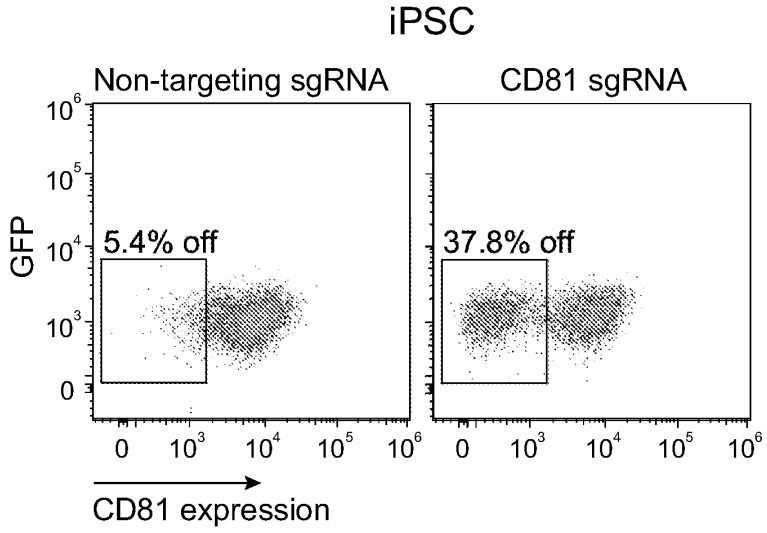

FIG. 9D

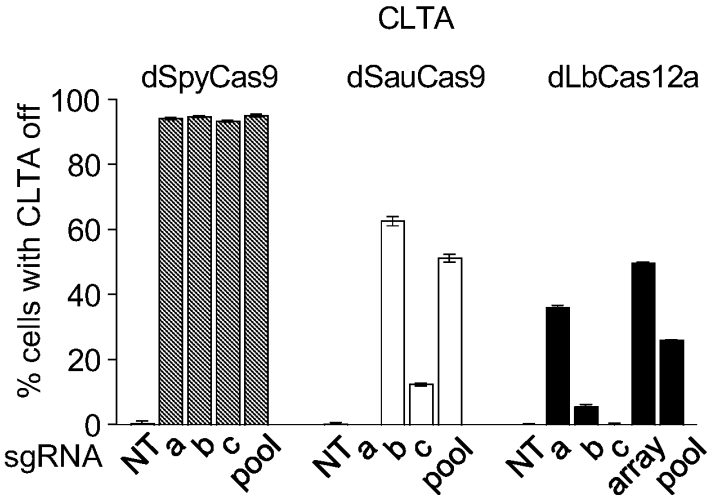
CLTA
dSpyCas9
dSauCas9
dLbCas12a
% cells with CLTA off
100
80
60
40
20
0
sgRNA
NT a b c pool
NT a b c pool
NT a b c array pool

FIG. 9E

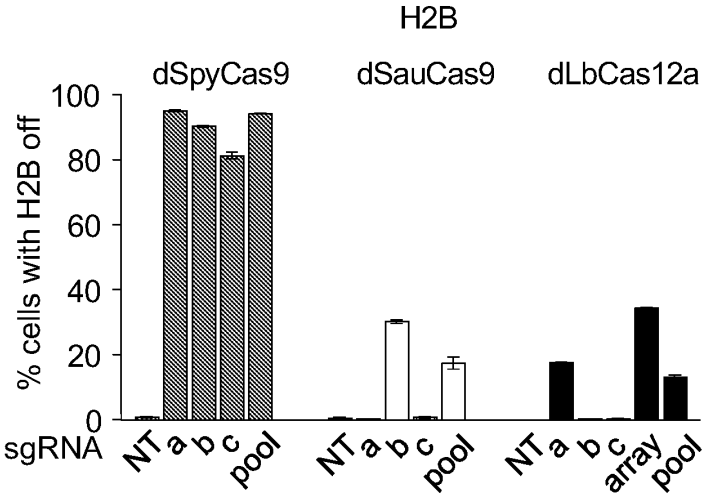
H2B
dSpyCas9
dSauCas9
dLbCas12a
% cells with H2B off
100
80
60
40
20
0
sgRNA
NT a b c pool
NT a b c pool
NT a b c array pool

FIG. 9F

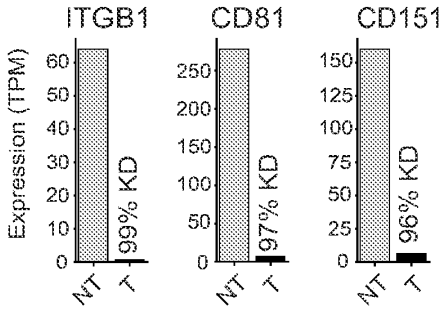

FIG. 10A

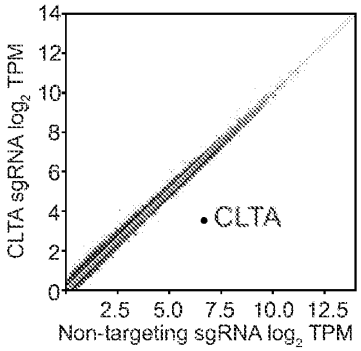

FIG. 10B

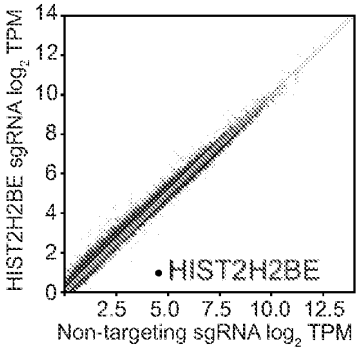

FIG. 10C

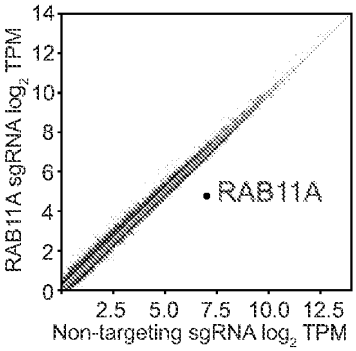

FIG. 10D

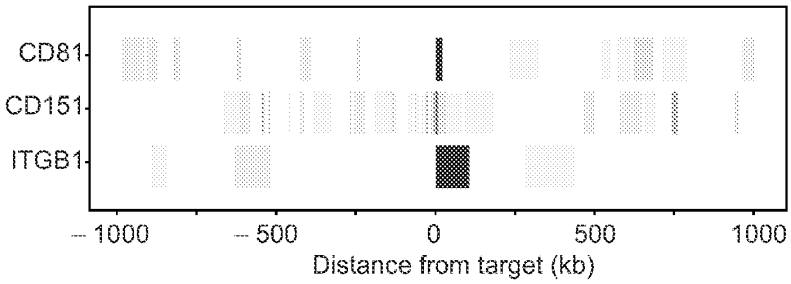

FIG. 10E

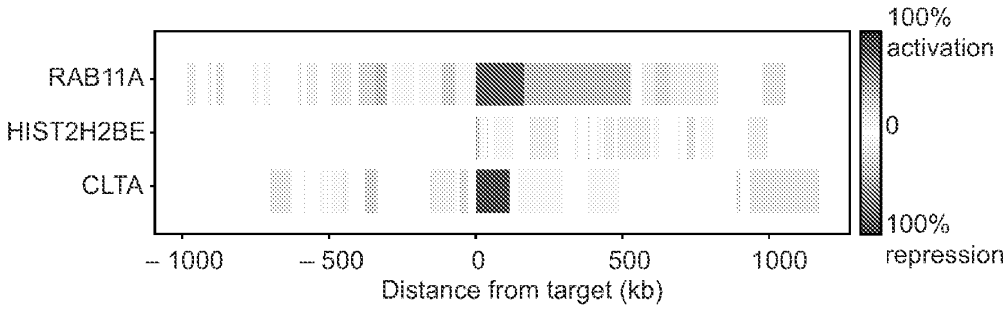

FIG. 10F

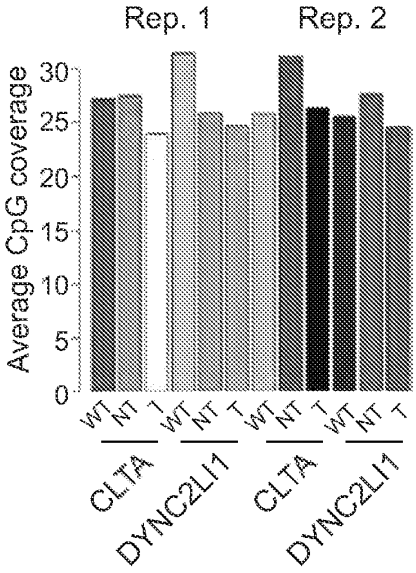

FIG. 10G

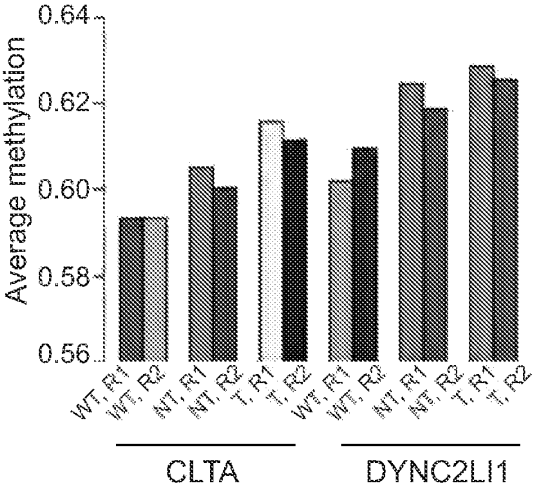

FIG. 10H

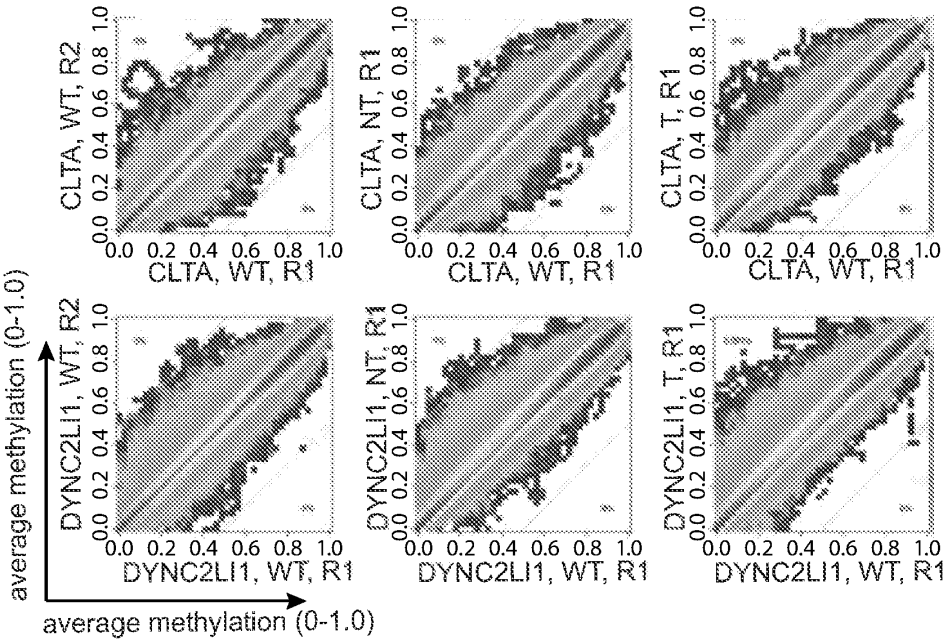

FIG. 10I

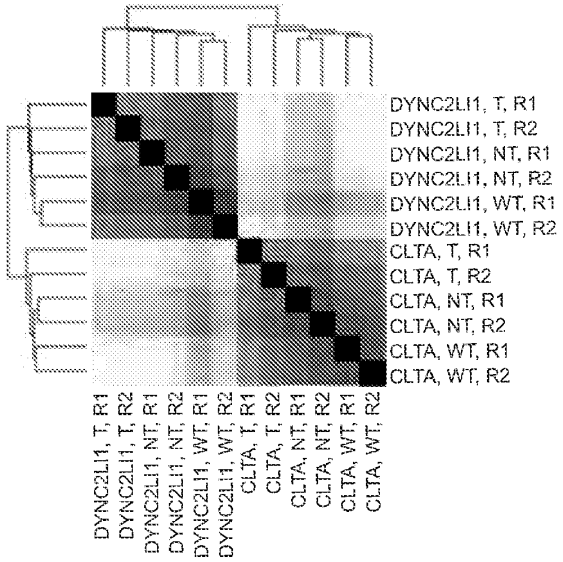

FIG. 10J

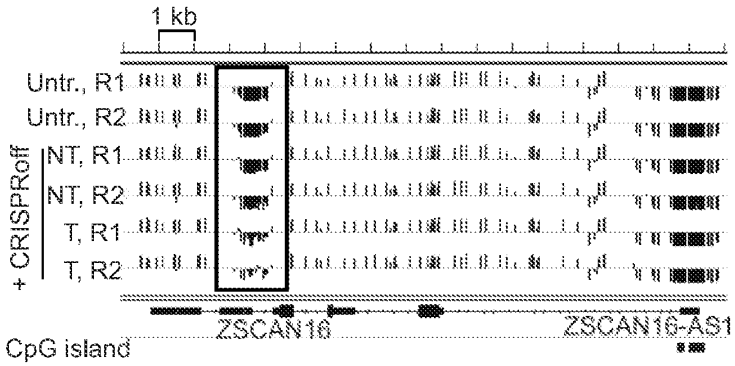

FIG. 10K

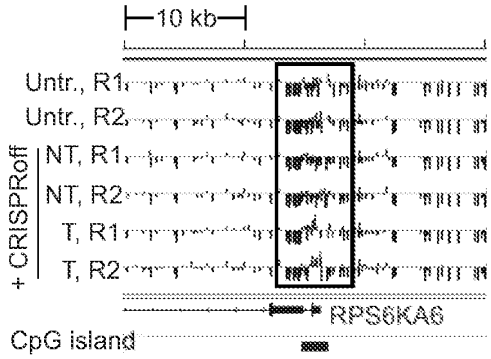

FIG. 10L

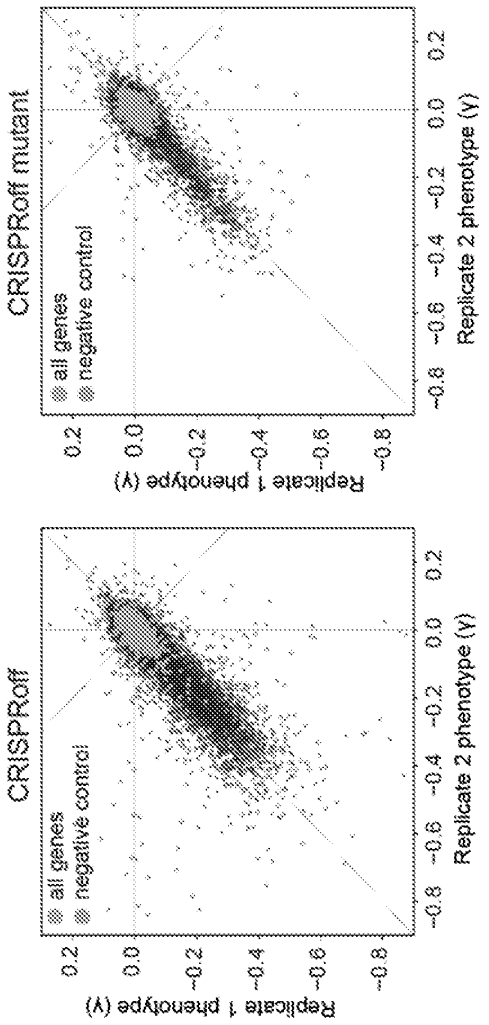

FIG. 11A

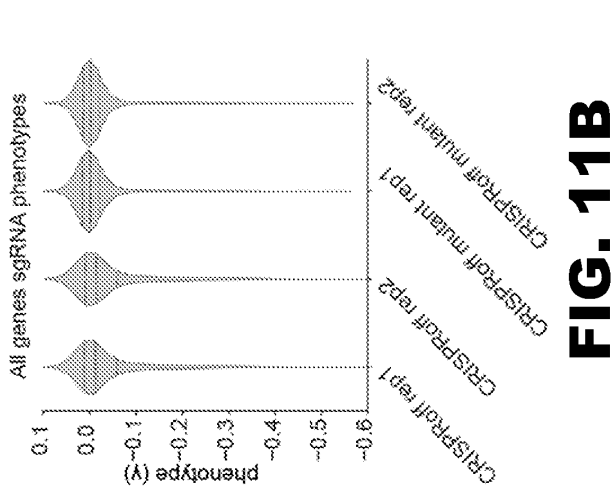

FIG. 11B

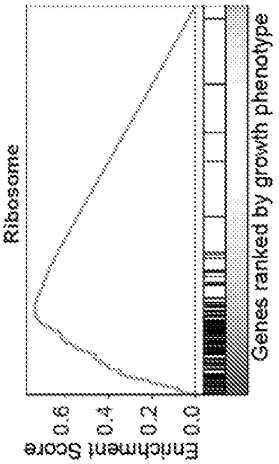

FIG. 11E

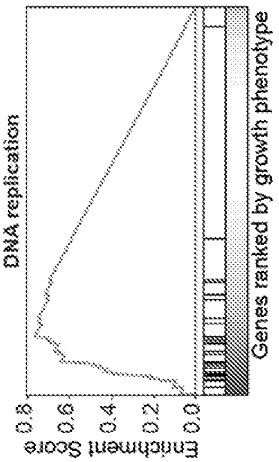

FIG. 11D

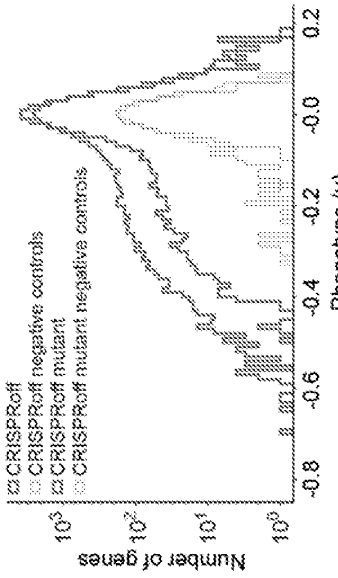

FIG. 11C

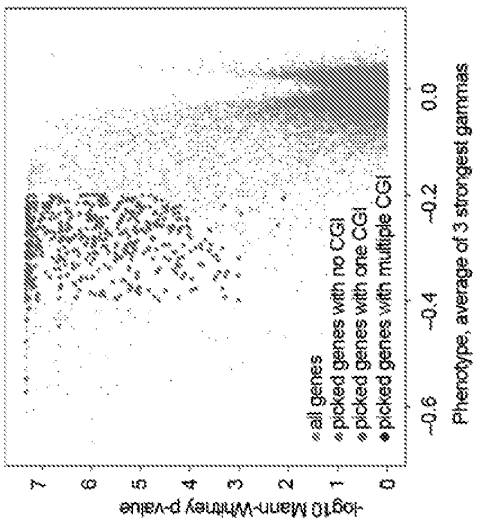

FIG. 12A

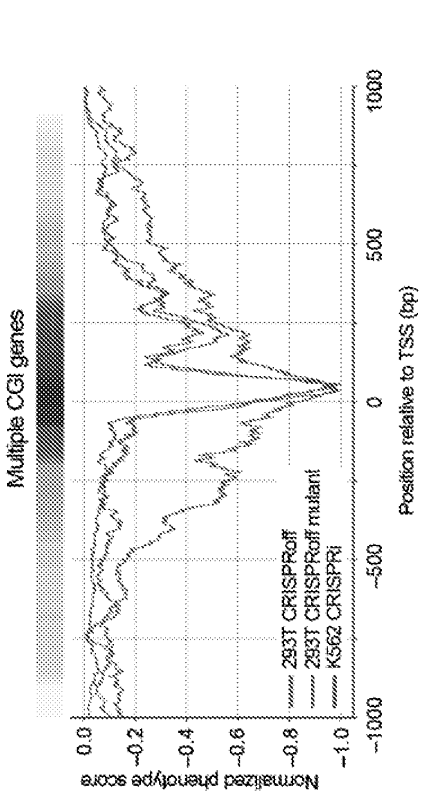

FIG. 12B

FIG. 12C

FIG. 12D

FIG. 12E

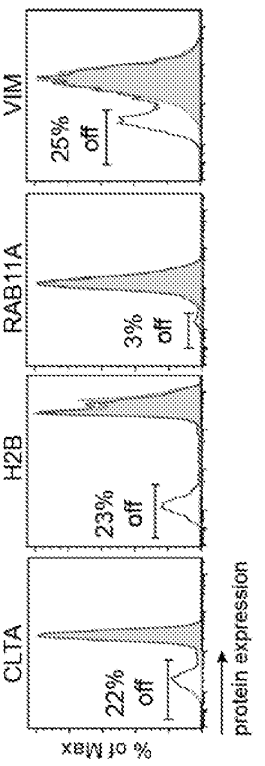

FIG. 12F

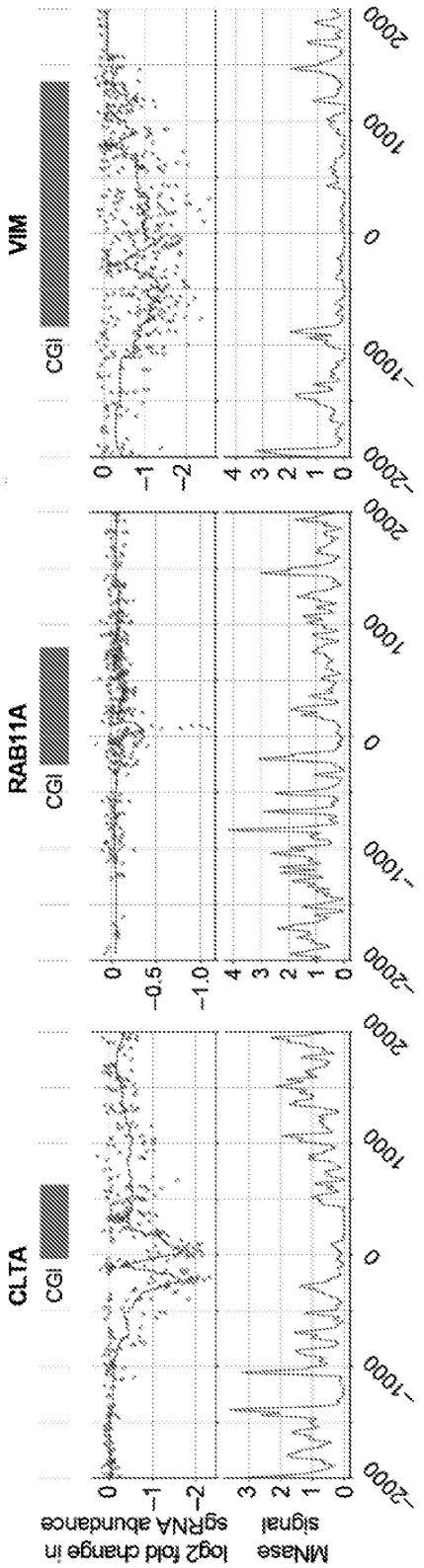

FIG. 12G

FIG. 12H

FIG. 12I

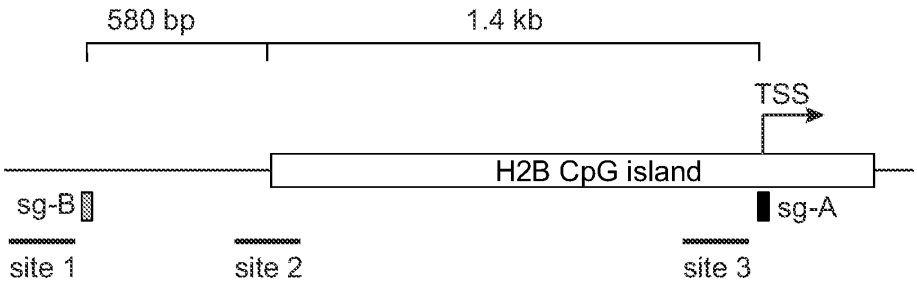

FIG. 13A

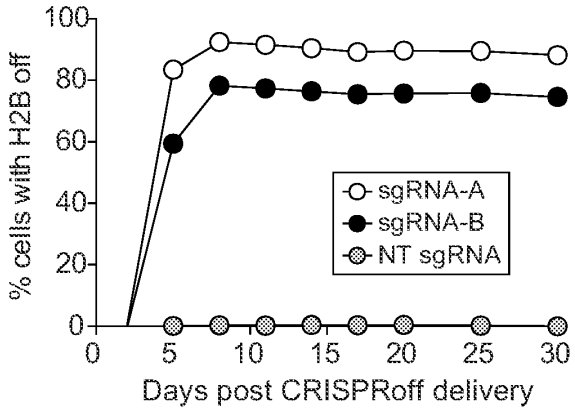

FIG. 13B

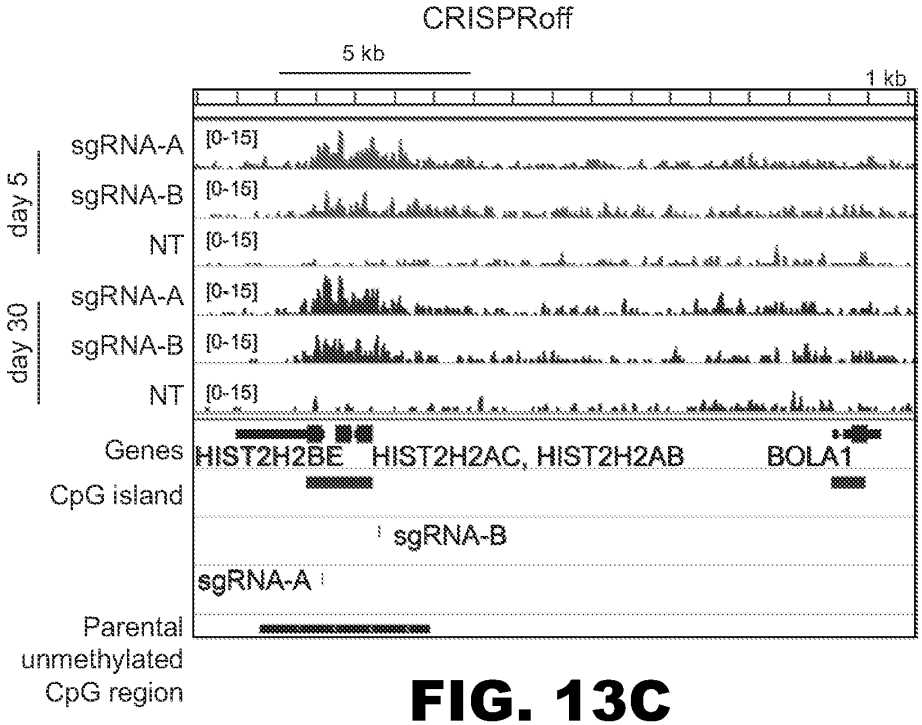

FIG. 13C

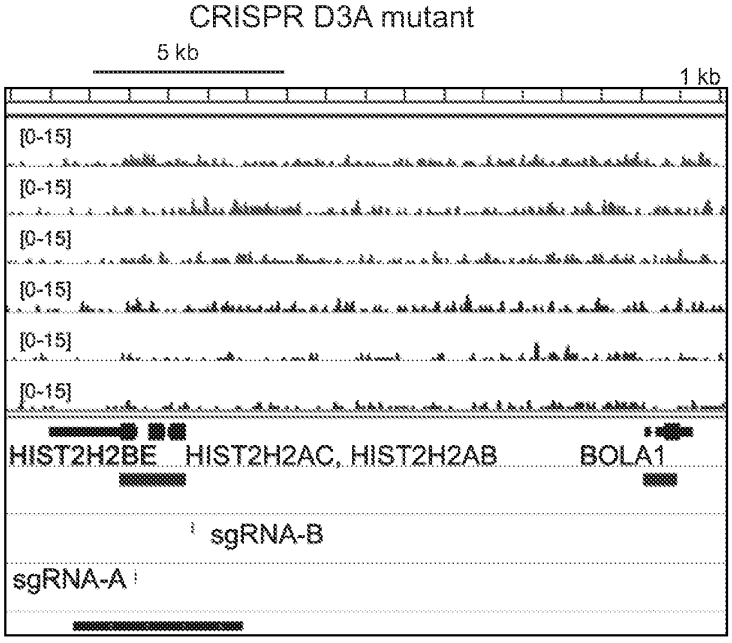

FIG. 13D

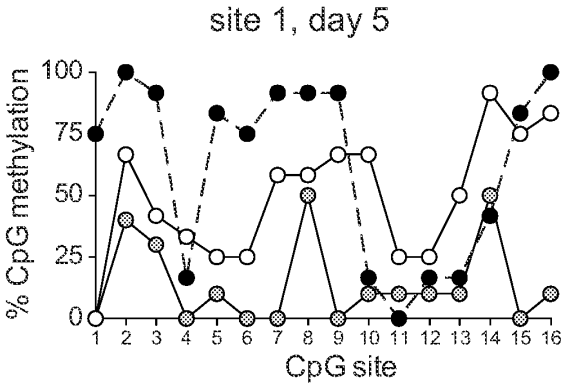

FIG. 13E

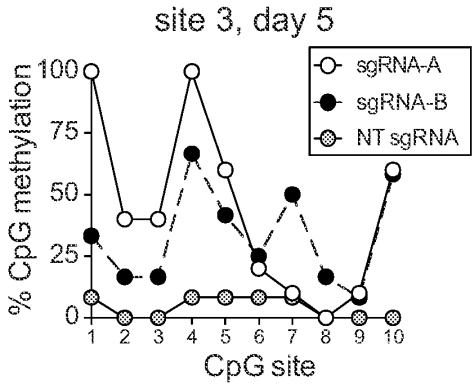

FIG. 13F

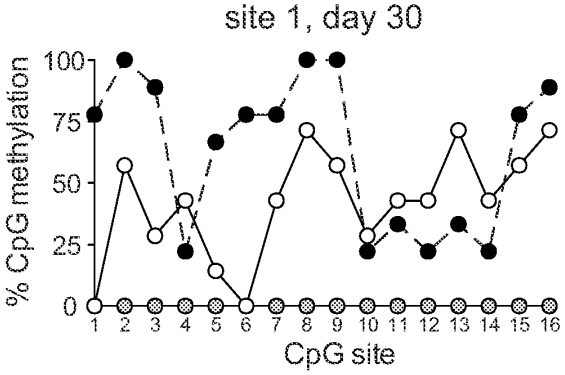

FIG. 13G

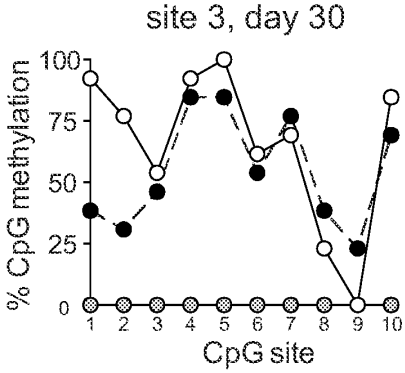

FIG. 13H

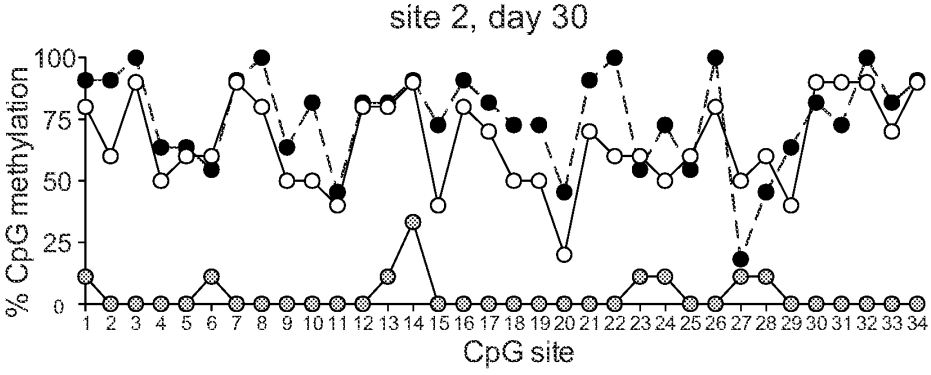

FIG. 13I