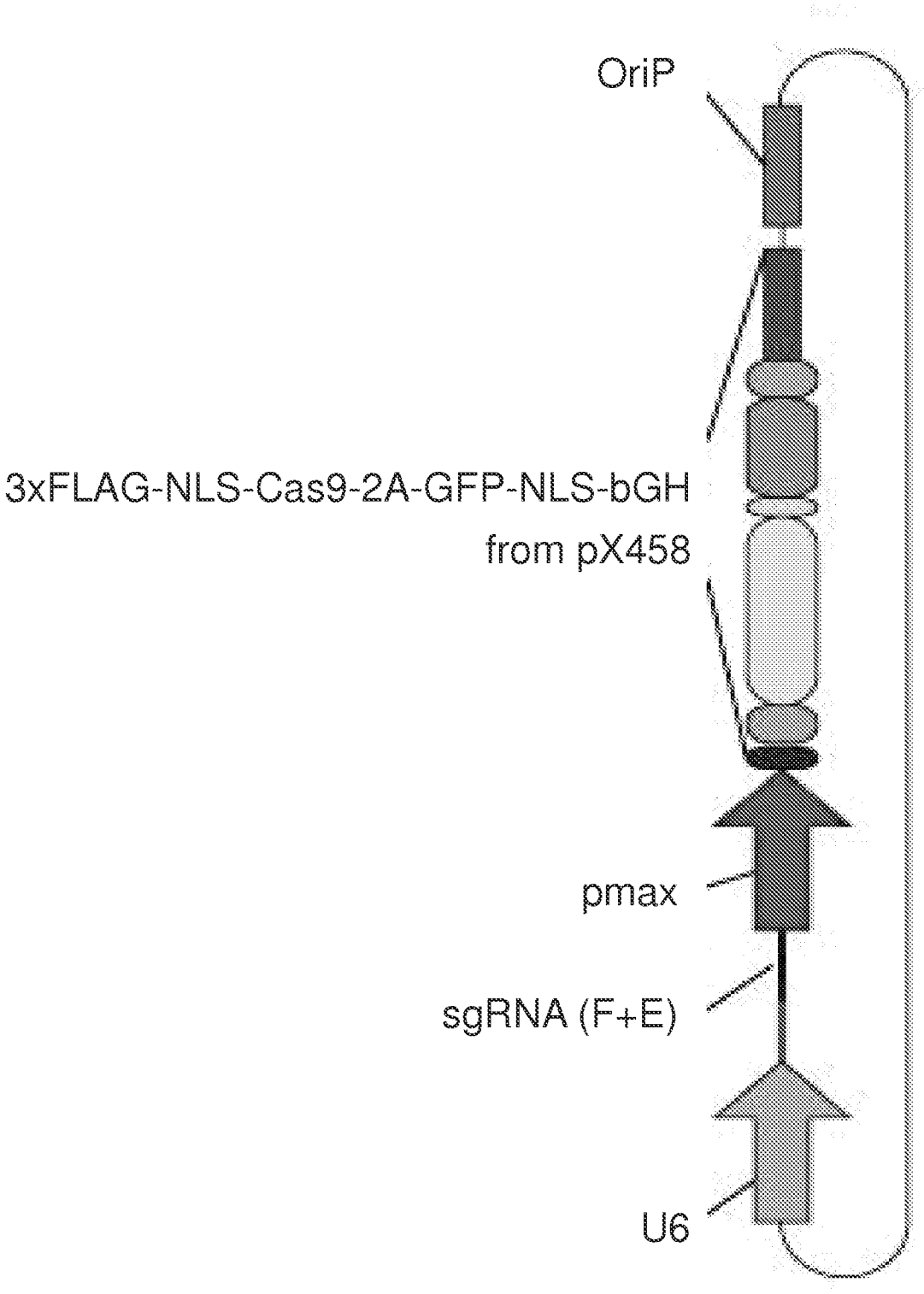

OriP
3xFLAG-NLS-Cas9-2A-GFP-NLS-bGH
from pX458
pmax
sgRNA (F+E)
U6

FIG. 1A

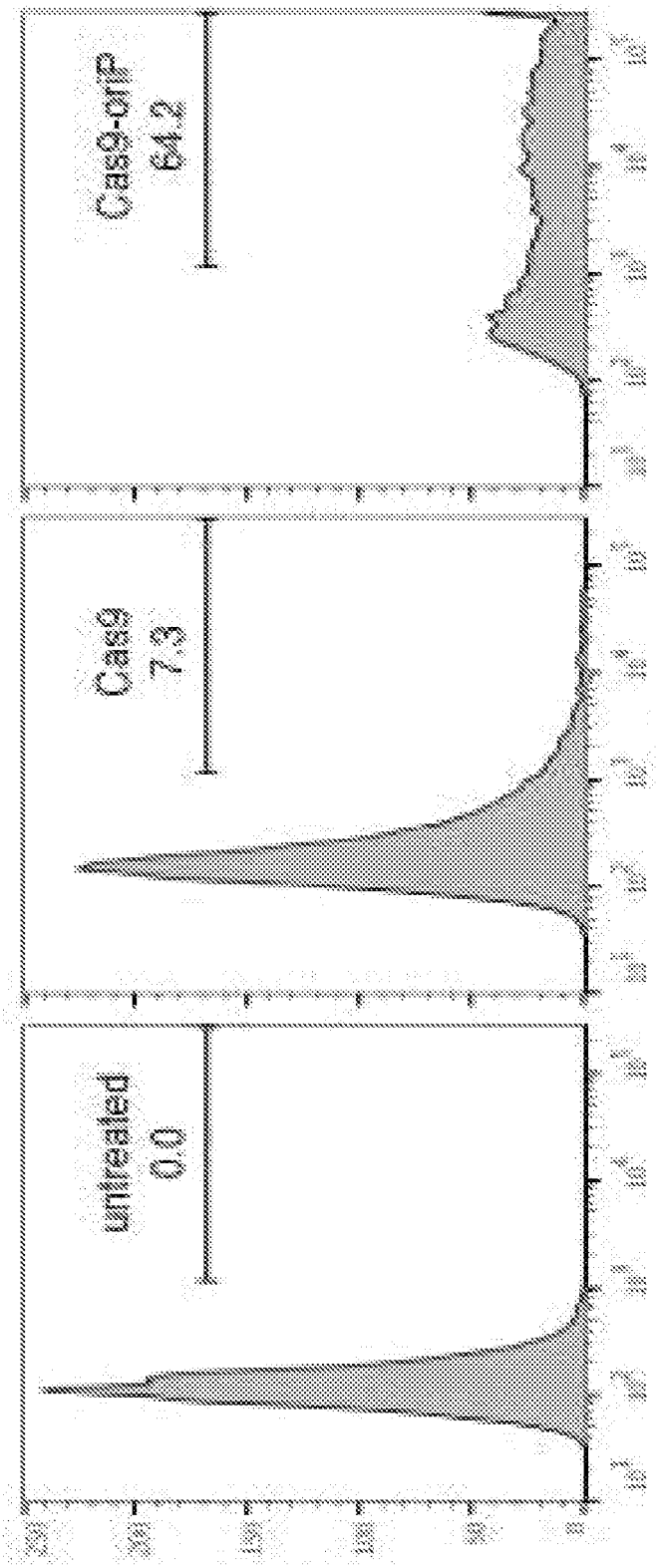


FIG. 1B

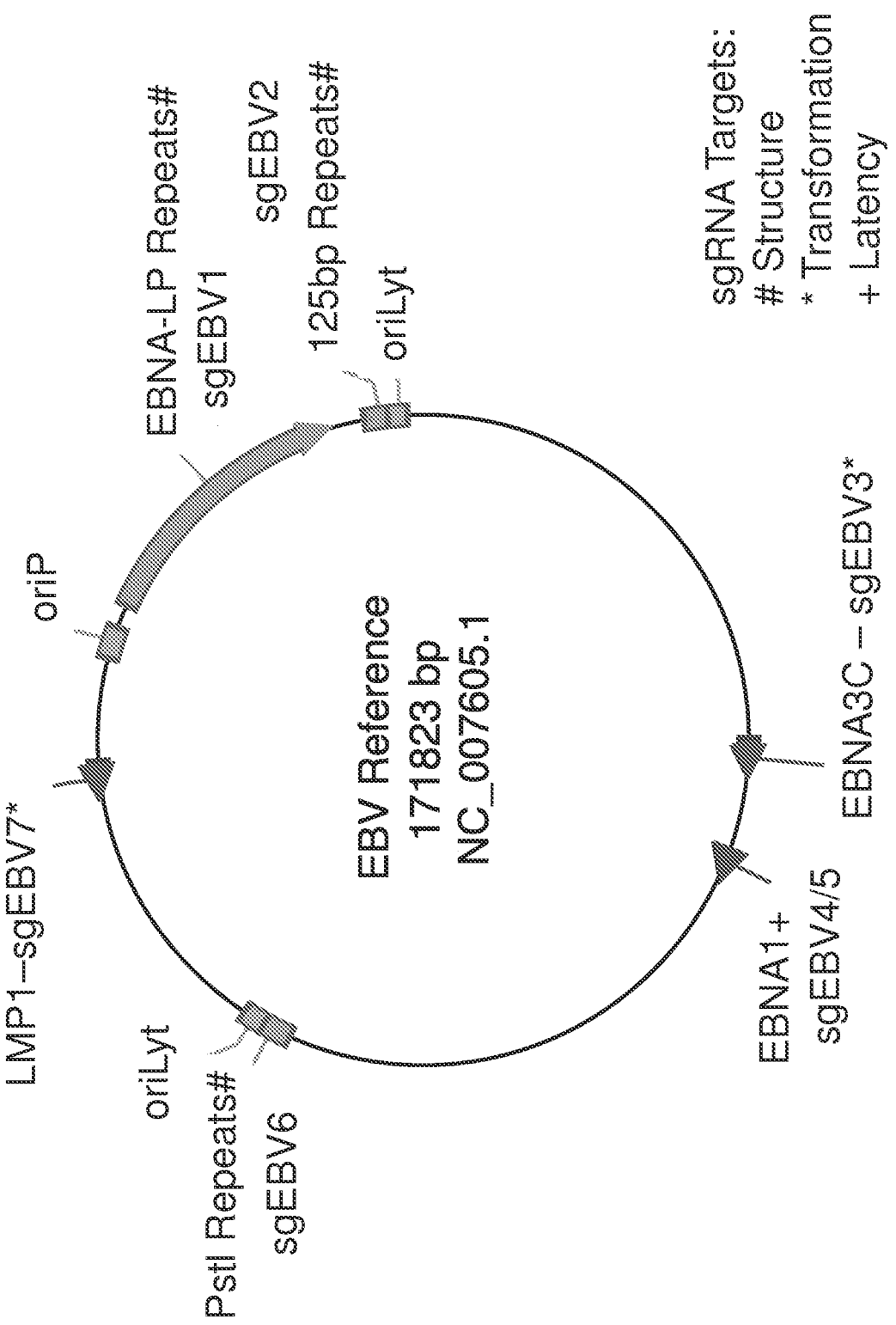

EBV Reference
171823 bp
NC_007605.1
oriP
EBNA-LP Repeats#
sgEBV1
sgEBV2
125bp Repeats#
oriLyt
sgRNA Targets:
Structure
* Transformation
+ Latency
EBNA3C – sgEBV3*
EBNA1+
sgEBV4/5
oriLyt
PstI Repeats#
sgEBV6
LMP1–sgEBV7*

FIG. 1C

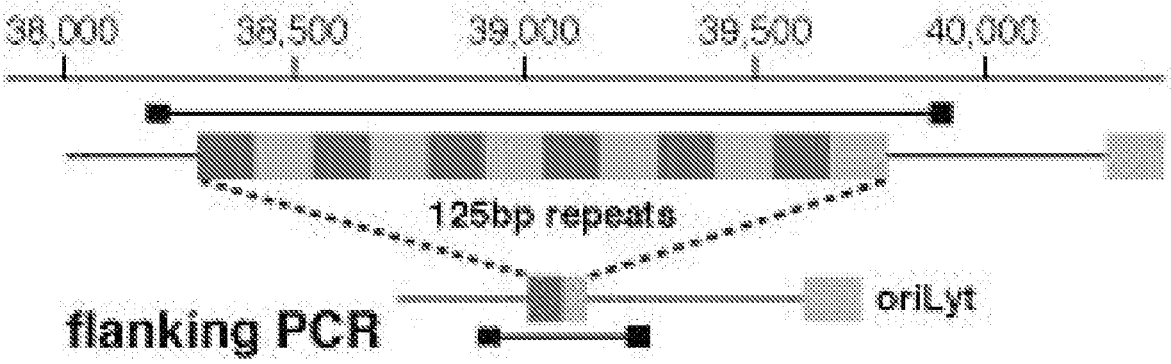

38,000
38,500
39,000
39,500
40,000
125bp repeats
oriLyt
flanking PCR

FIG. 2A

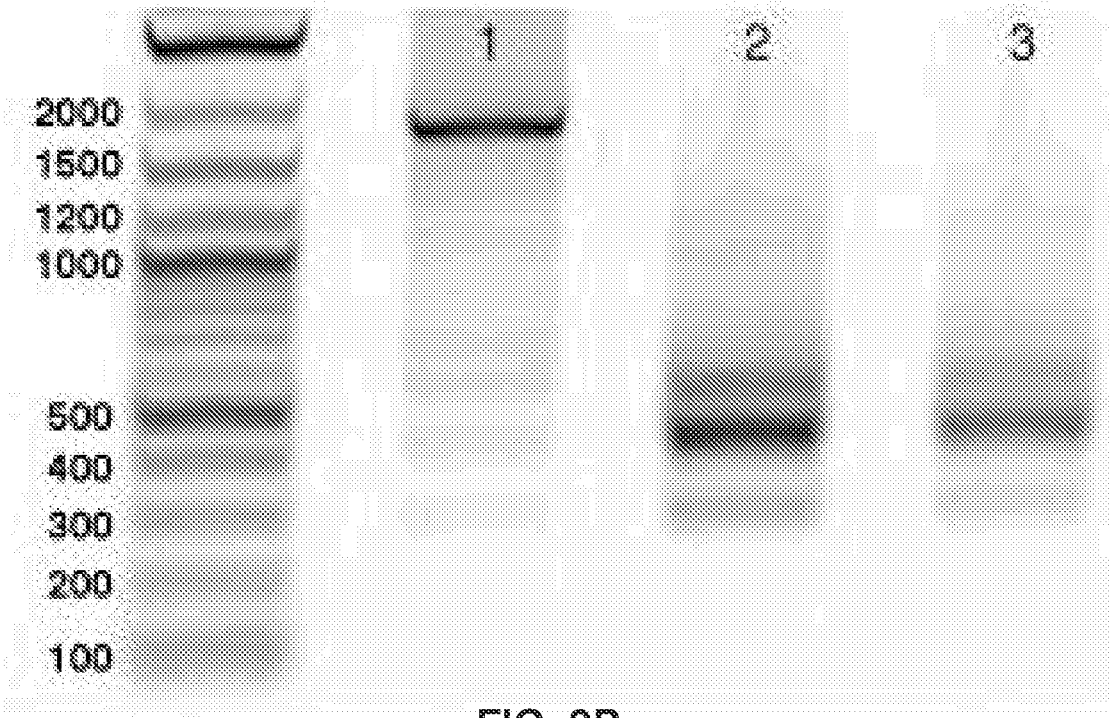

1
2
3
2000
1500
1200
1000
500
400
300
200
100

FIG. 2B

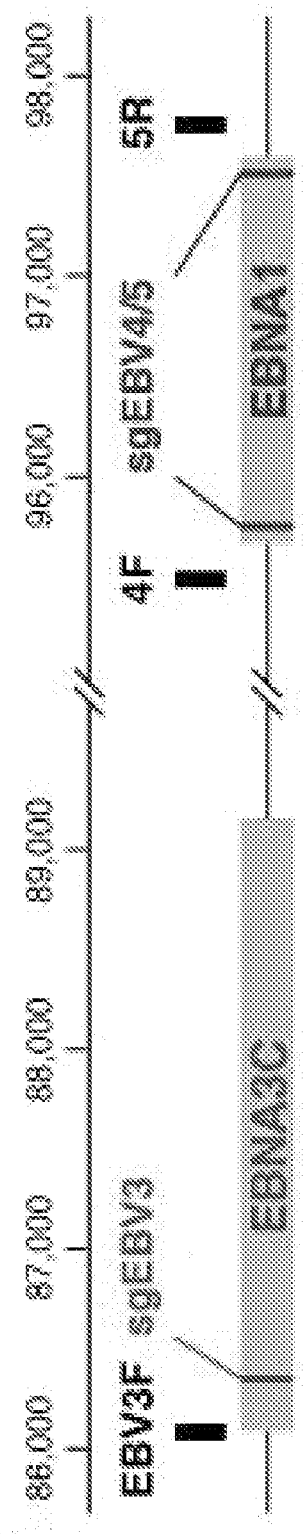

86,000
87,000
88,000
89,000
96,000
97,000
98,000
EBV3F
sgEBV3
4F
sgEBV4/5
5R
EBNA3C
EBNA1

FIG. 2C

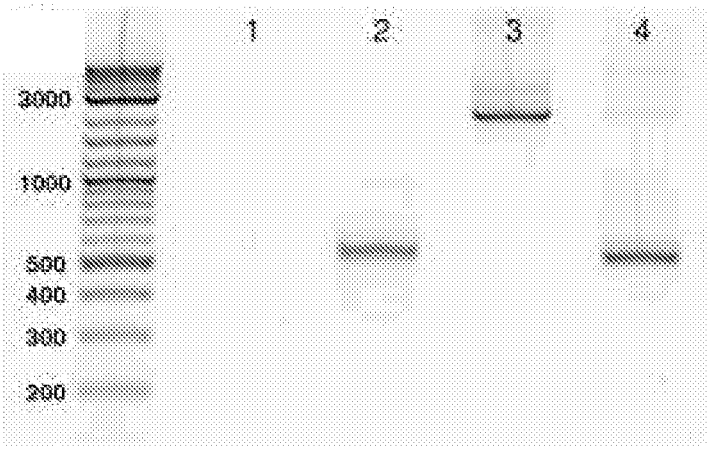


FIG. 2D

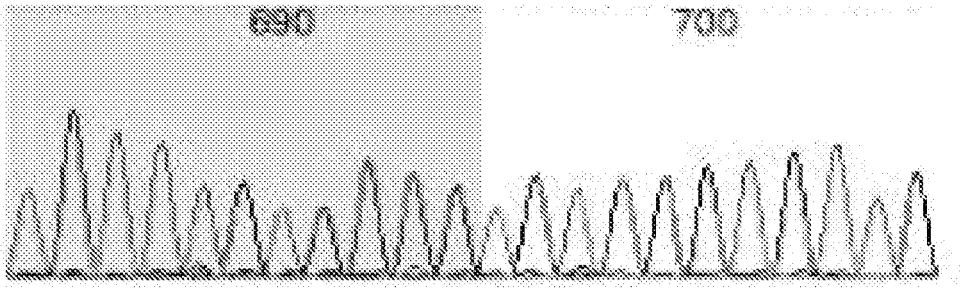


FIG. 2E

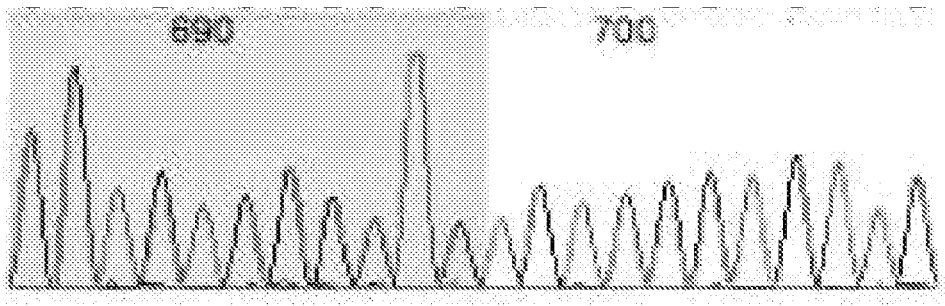


FIG. 2F

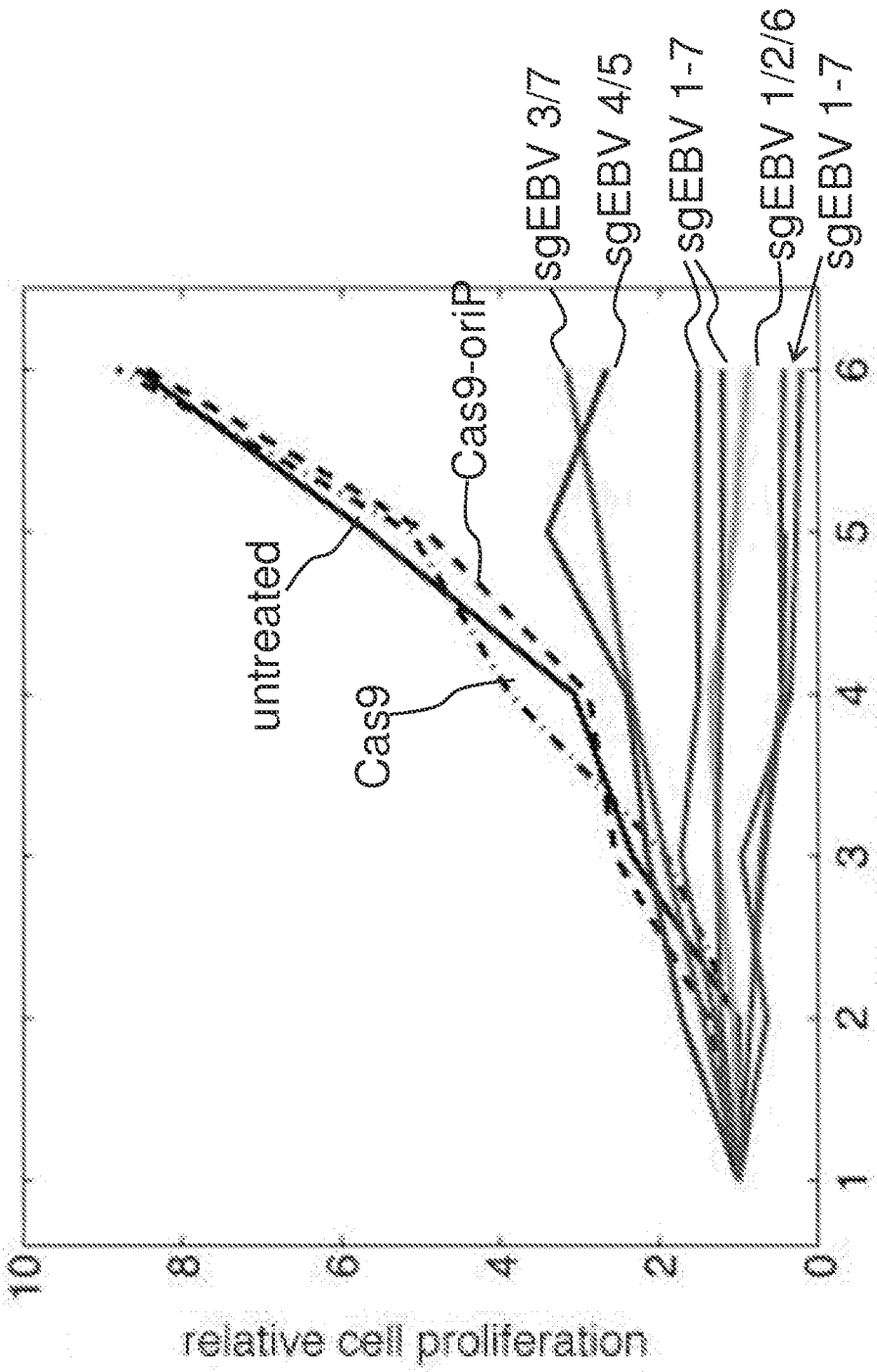

relative cell proliferation
0
2
4
6
8
10
days after flow sorting
1
2
3
4
5
6
untreated
Cas9
Cas9-oriP
sgEBV 3/7
sgEBV 4/5
sgEBV 1-7
sgEBV 1/2/6
sgEBV 1-7

FIG. 3A

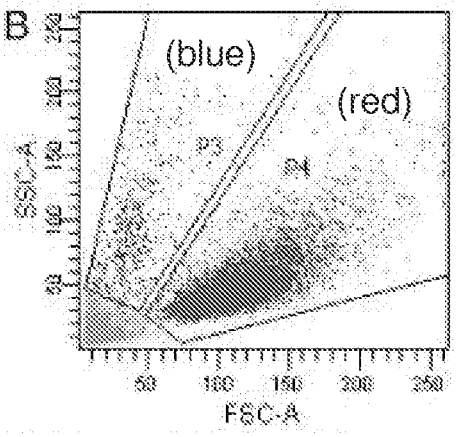


FIG. 3B

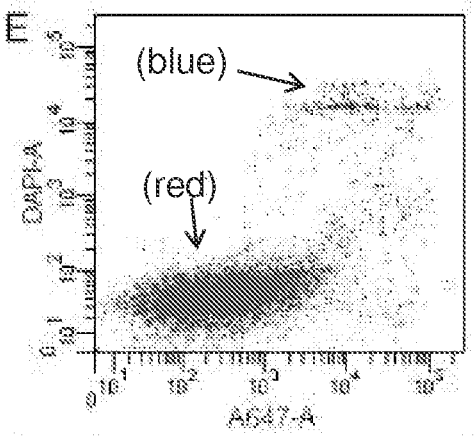


FIG. 3E

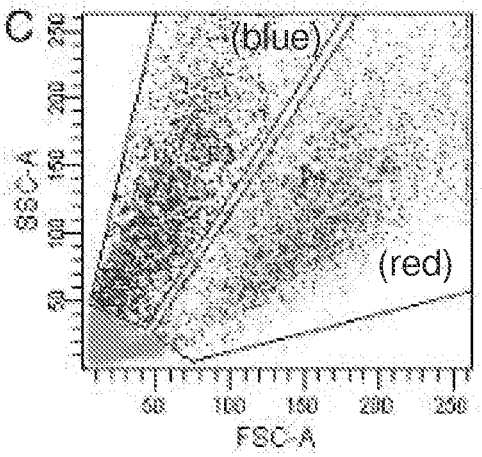


FIG. 3C

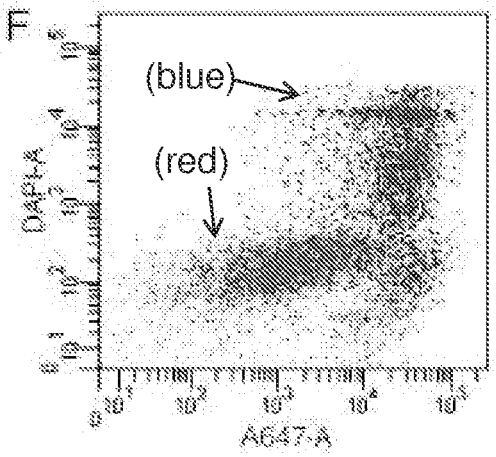


FIG. 3F

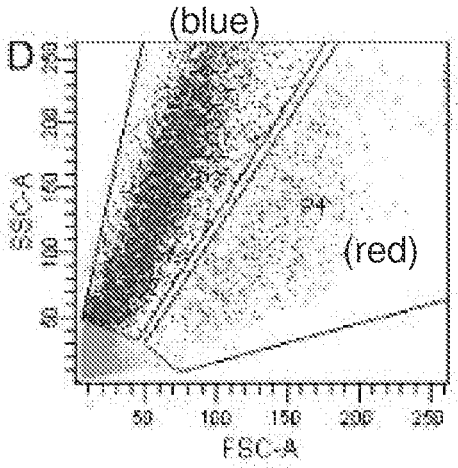


FIG. 3D

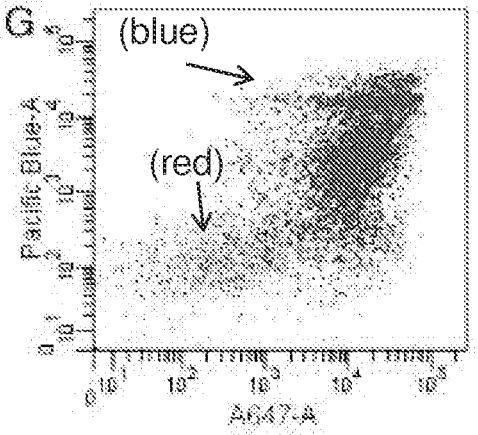


FIG. 3G

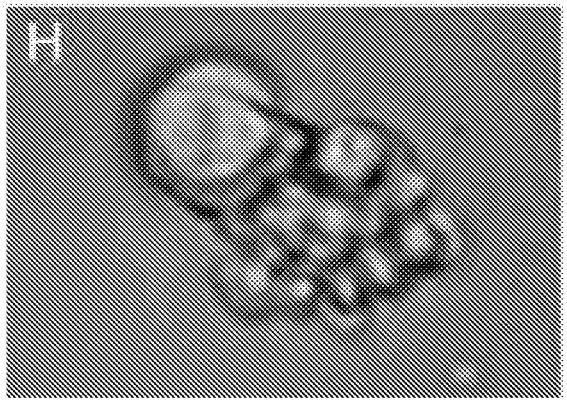


FIG. 3H

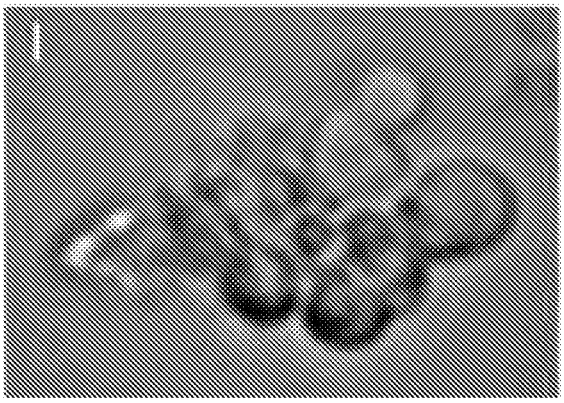


FIG. 3I

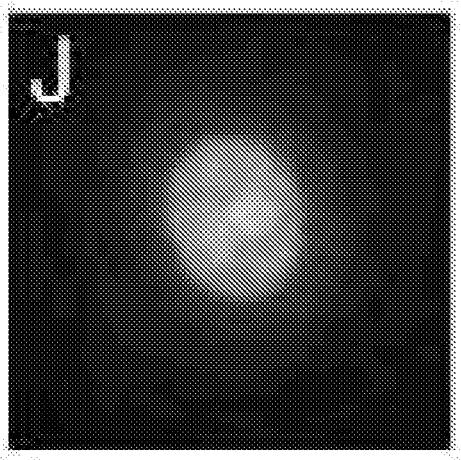


FIG. 3J

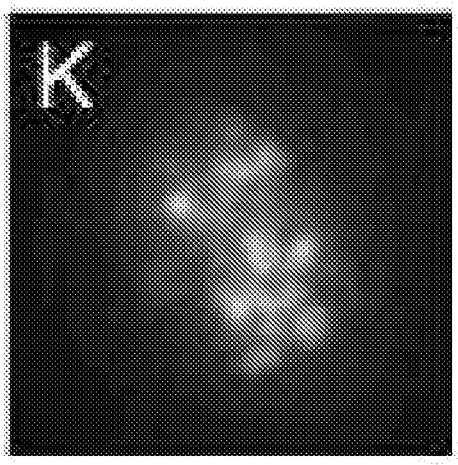


FIG. 3K

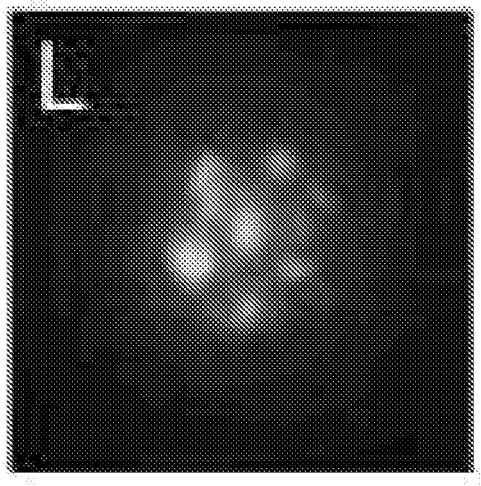


FIG. 3L

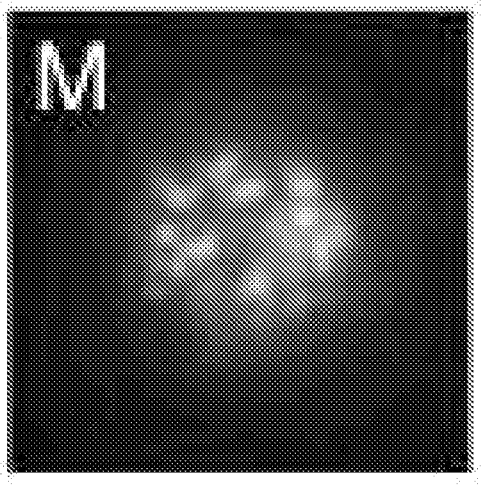


FIG. 3M

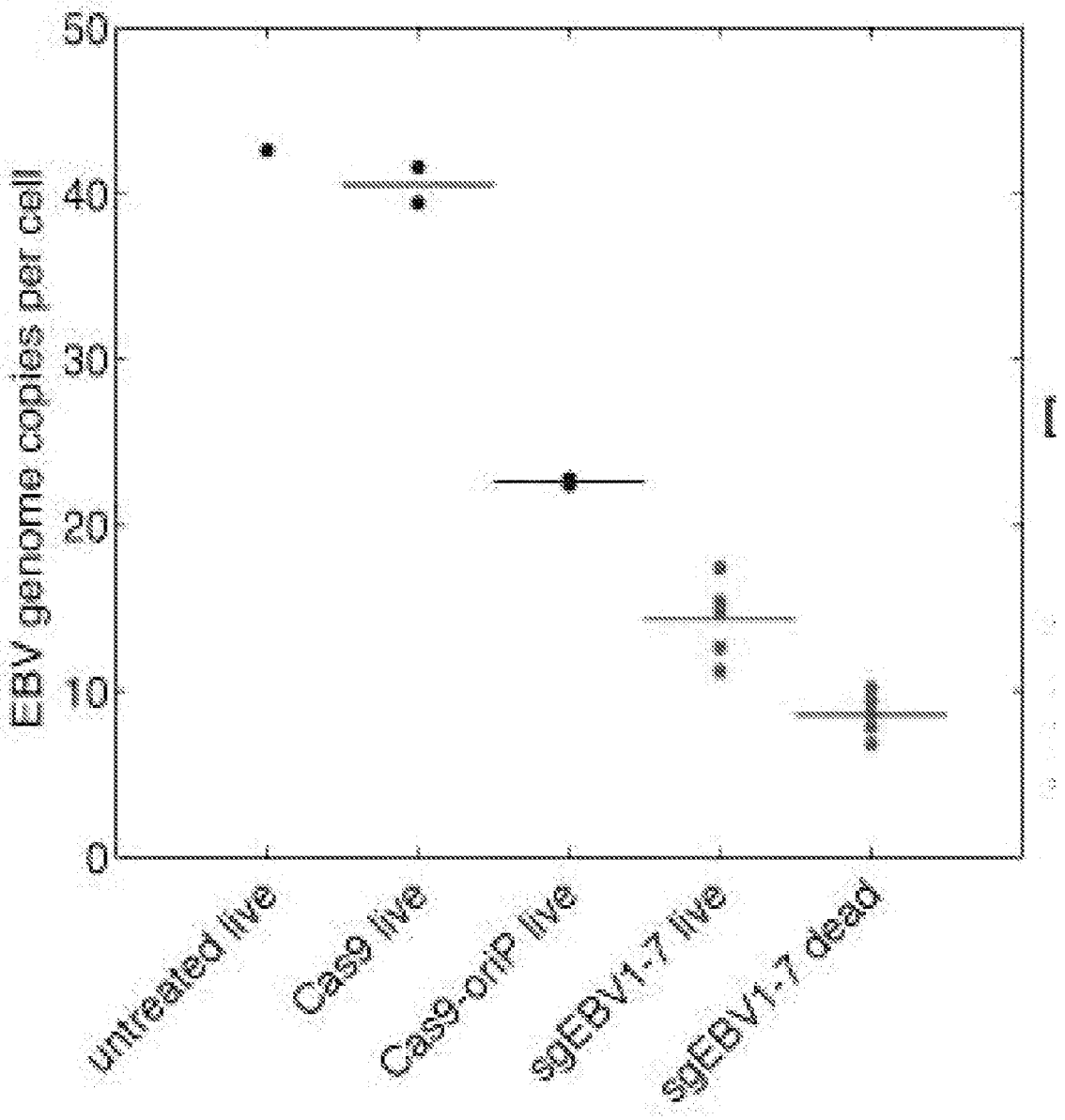

EBV genome copies per cell
50
40
30
20
10
0
untreated live
Cas9 live
Cas9-oriP live
sgEBV1-7 live
sgEBV1-7 dead

FIG. 4A

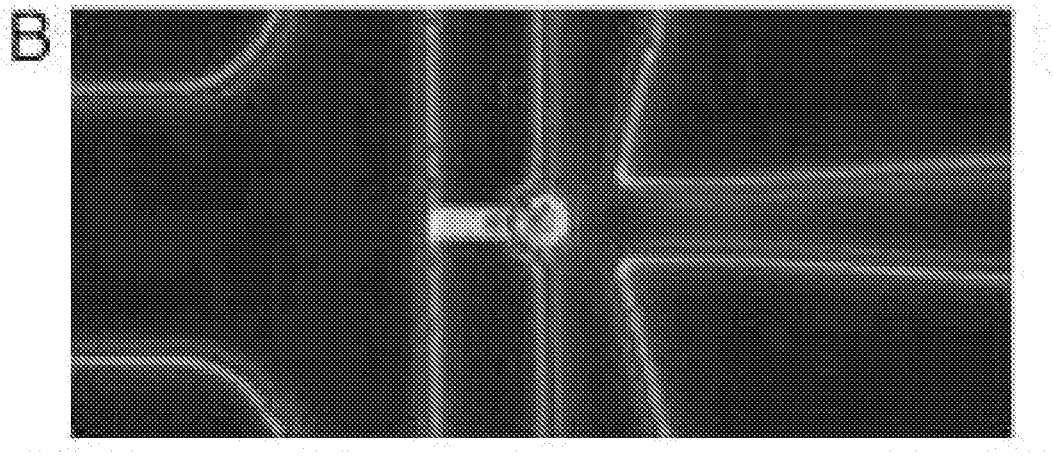


FIG. 4B

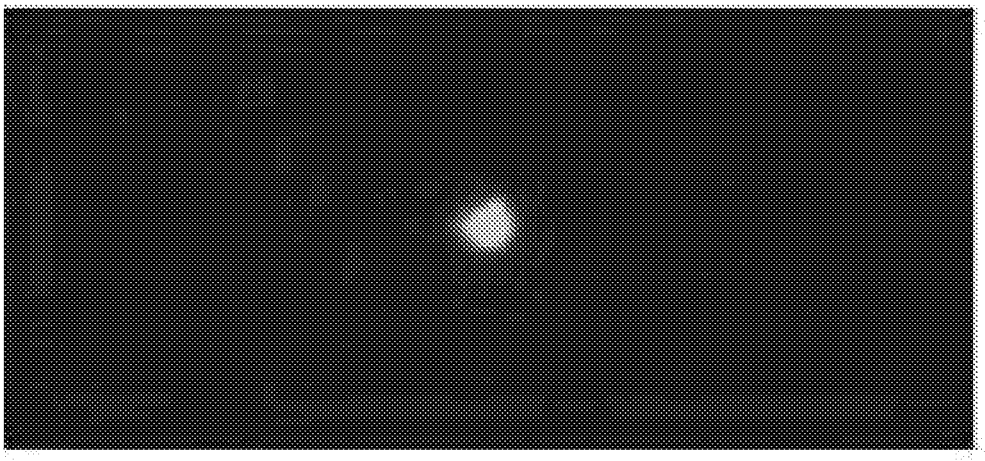


FIG. 4C

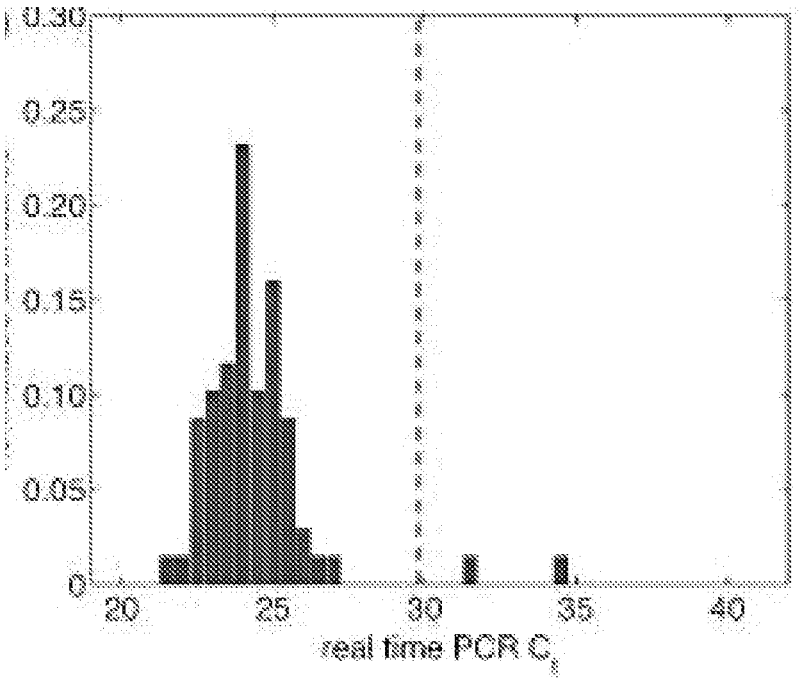

0.30
0.25
0.20
0.15
0.10
0.05
0
20
25
30
35
40
real time PCR C_t

FIG. 4D

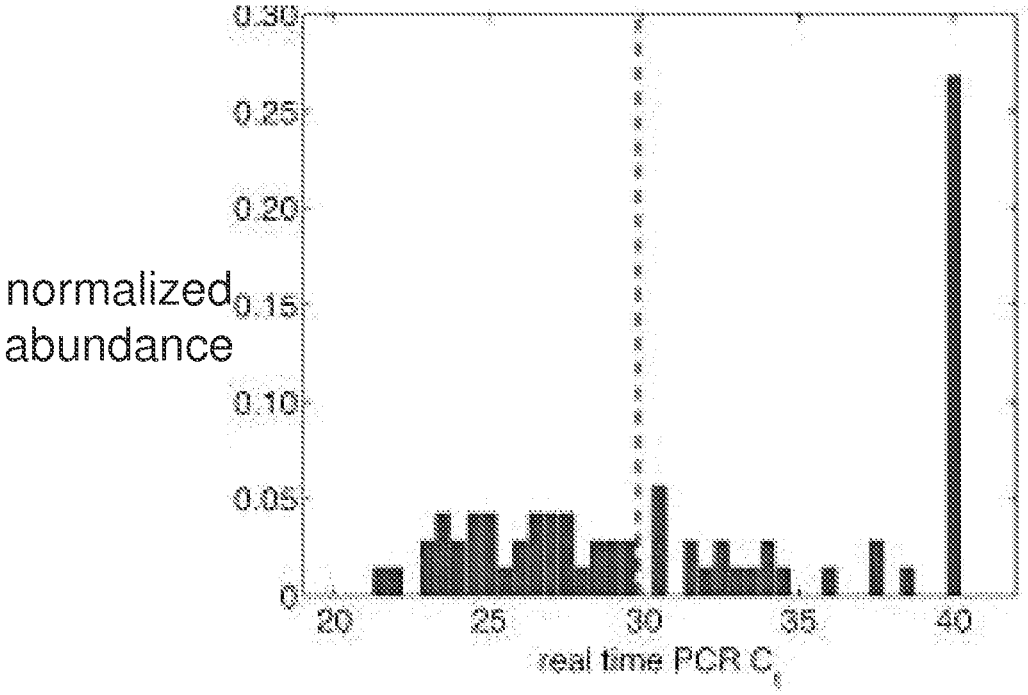

normalized abundance
0.30
0.25
0.20
0.15
0.10
0.05
0
20
25
30
35
40
real time PCR C_t

FIG. 4E

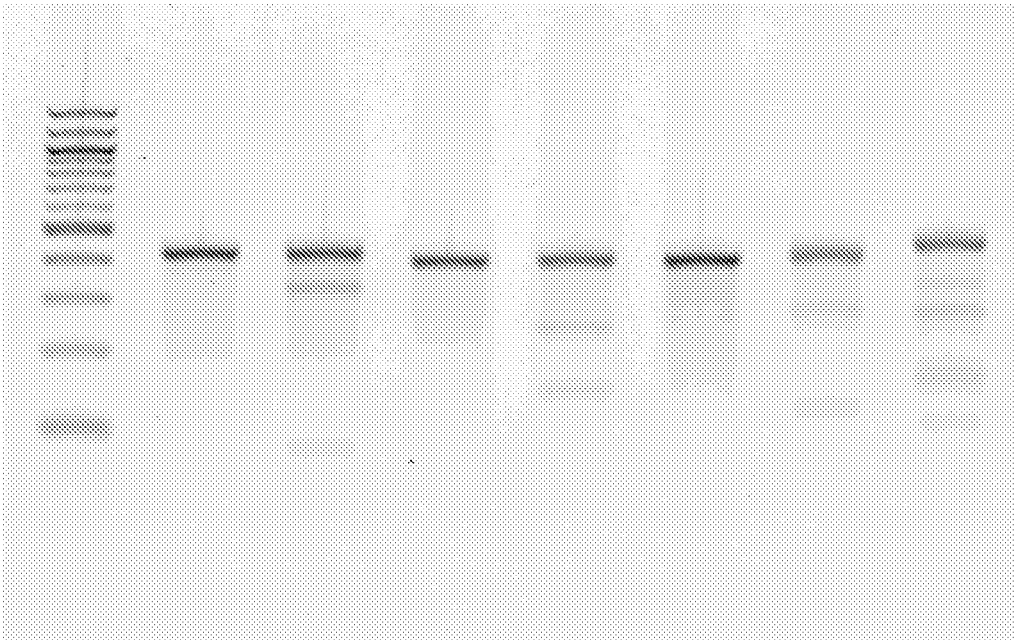


FIG. 5

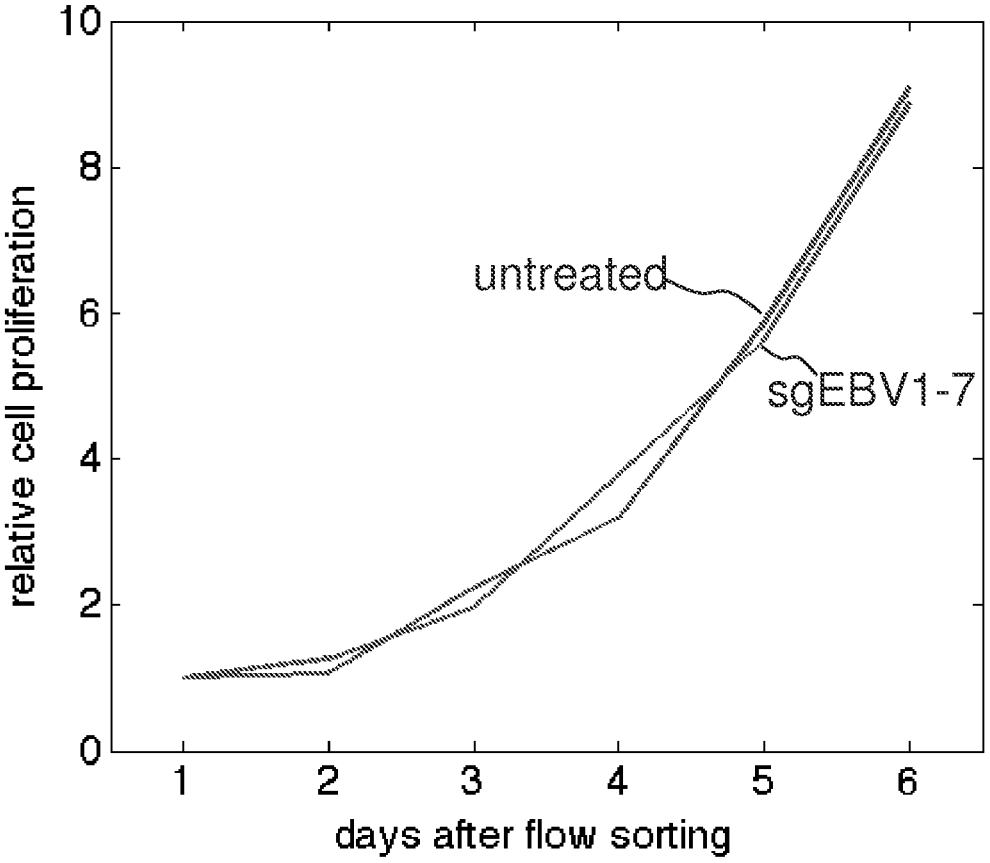

10
8
6
4
2
0
relative cell proliferation
untreated
sgEBV1-7
1
2
3
4
5
6
days after flow sorting

FIG. 6

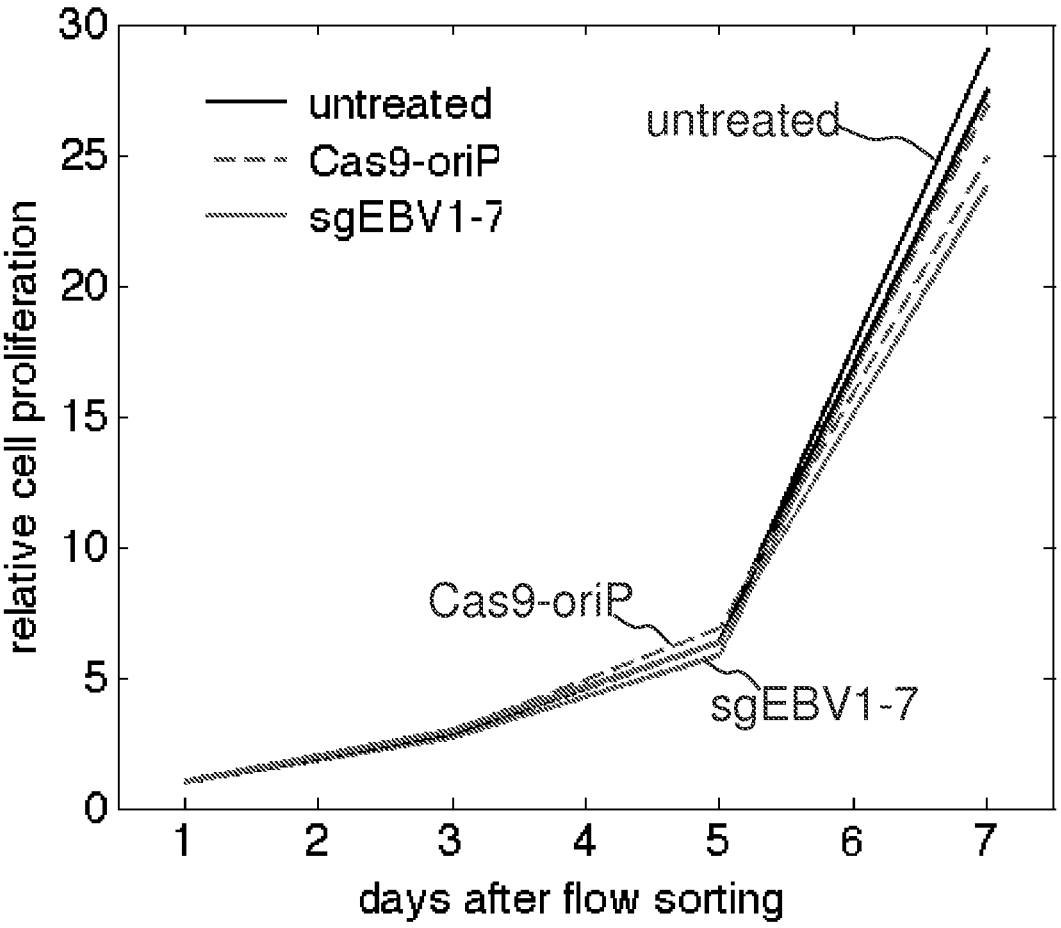

untreated
Cas9-oriP
sgEBV1-7
untreated
Cas9-oriP
sgEBV1-7
relative cell proliferation
days after flow sorting
0
5
10
15
20
25
30
1
2
3
4
5
6
7

FIG. 7

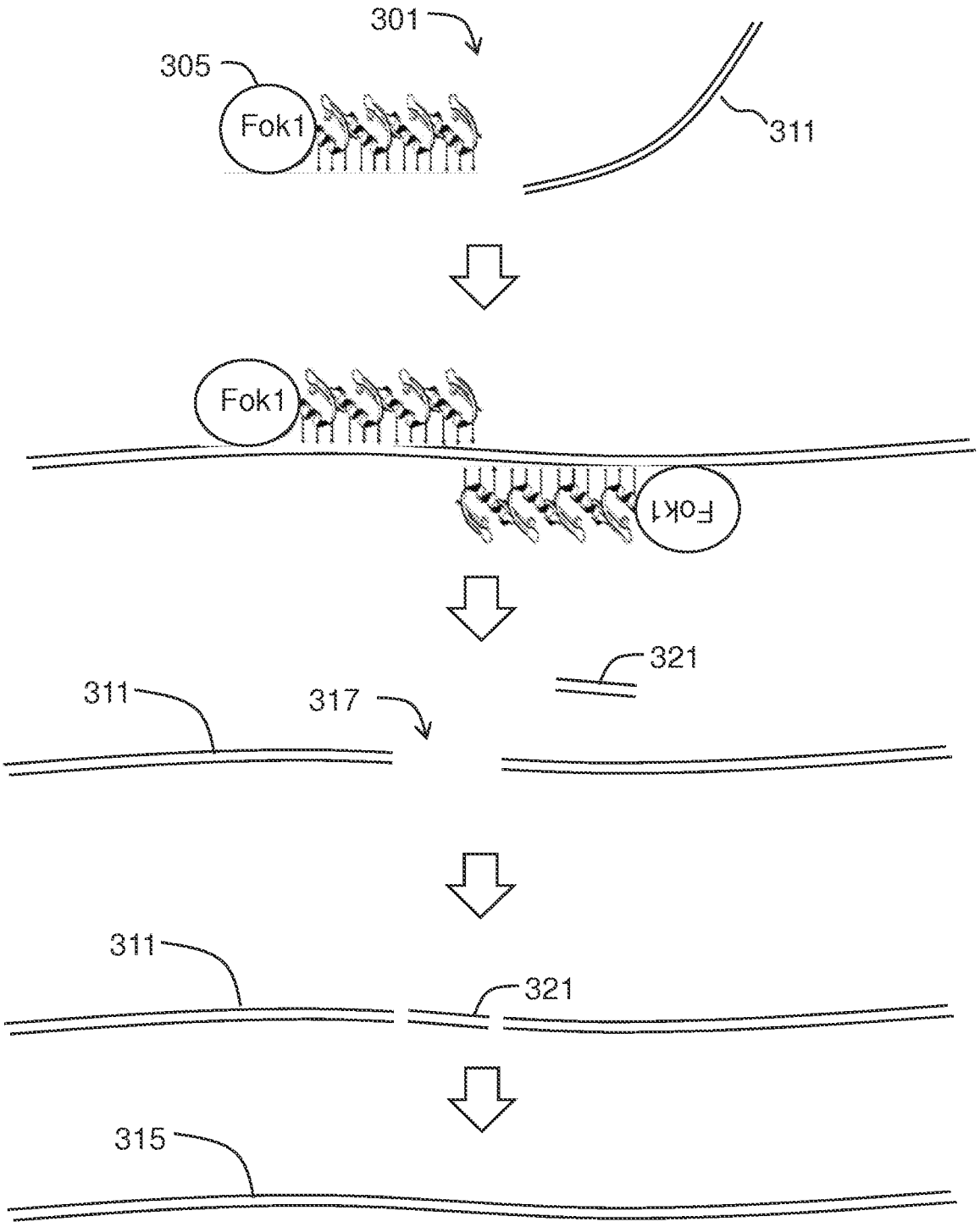


FIG. 8

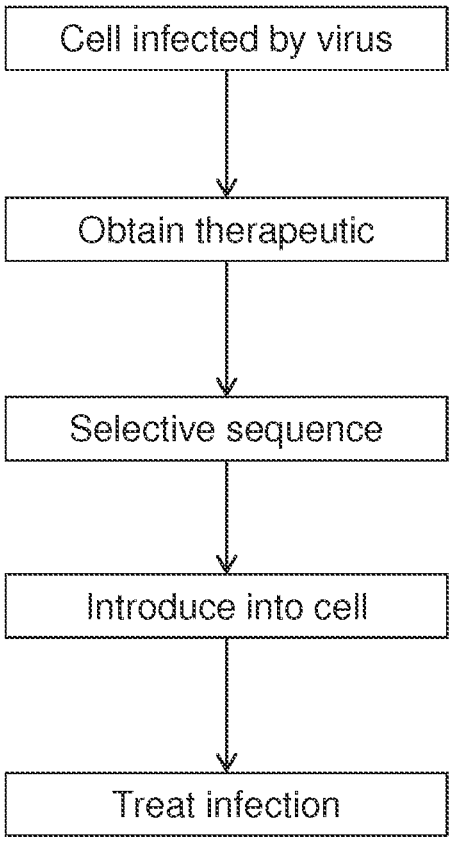

Cell infected by virus
Obtain therapeutic
Selective sequence
Introduce into cell
Treat infection

FIG. 9

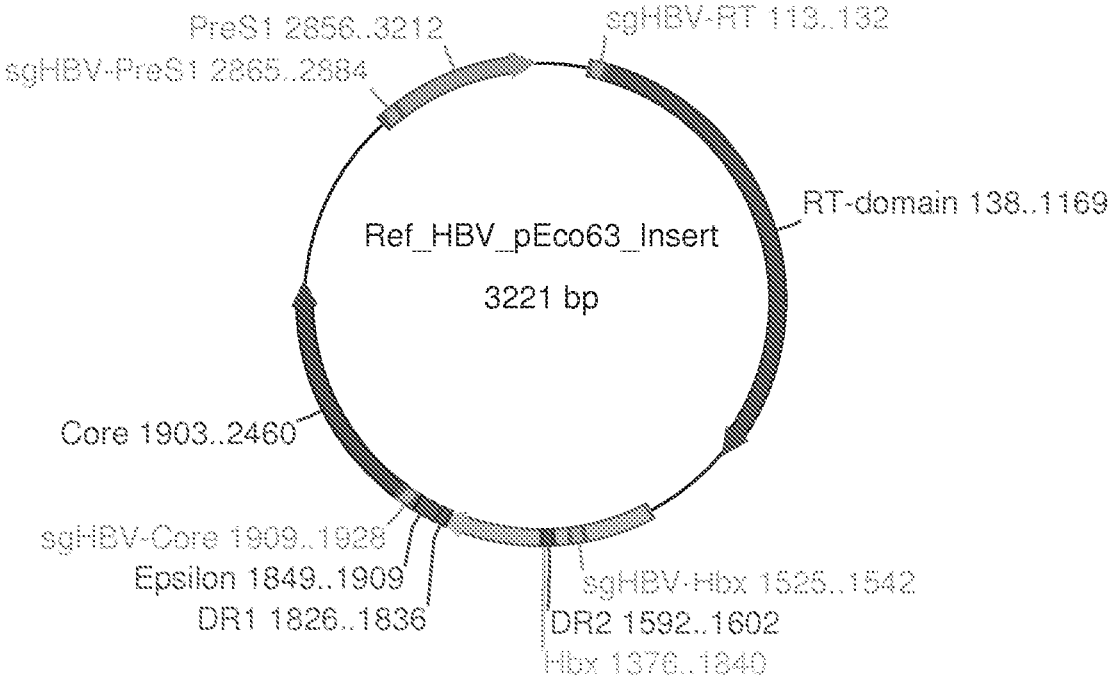

PreS1 2656..3212
sgHBV-PreS1 2865..2884
sgHBV-RT 113..132
RT-domain 138..1169
Ref_HBV_pEco63_Insert
3221 bp
Core 1903..2460
sgHBV-Core 1909..1928
Epsilon 1849..1909
DR1 1826..1836
sgHBV-Hbx 1525..1542
DR2 1592..1602
Hbx 1376..1840

FIG. 10

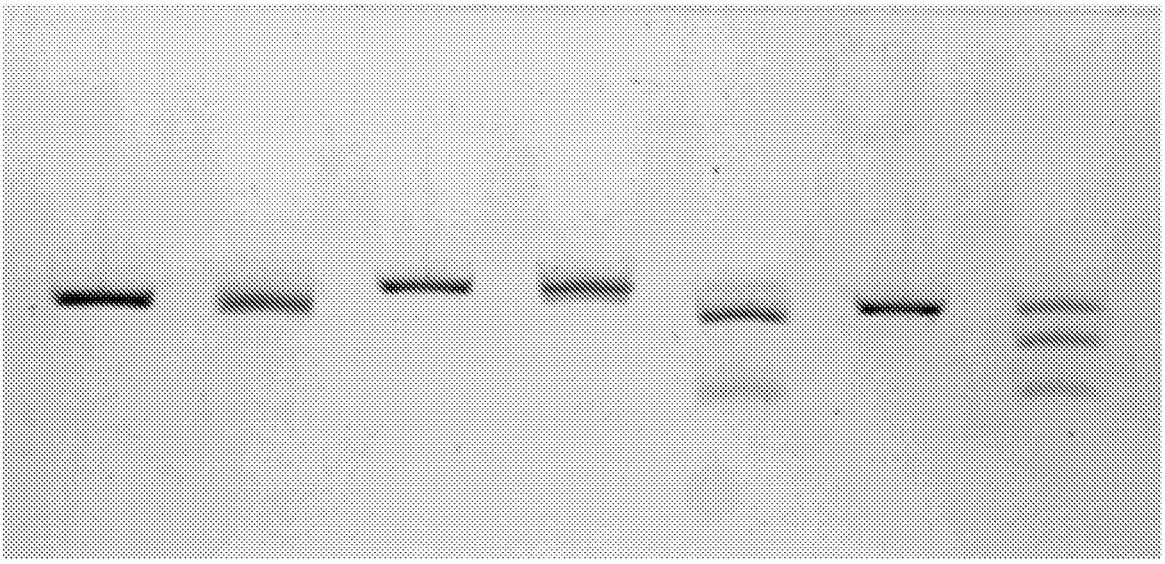


FIG. 11

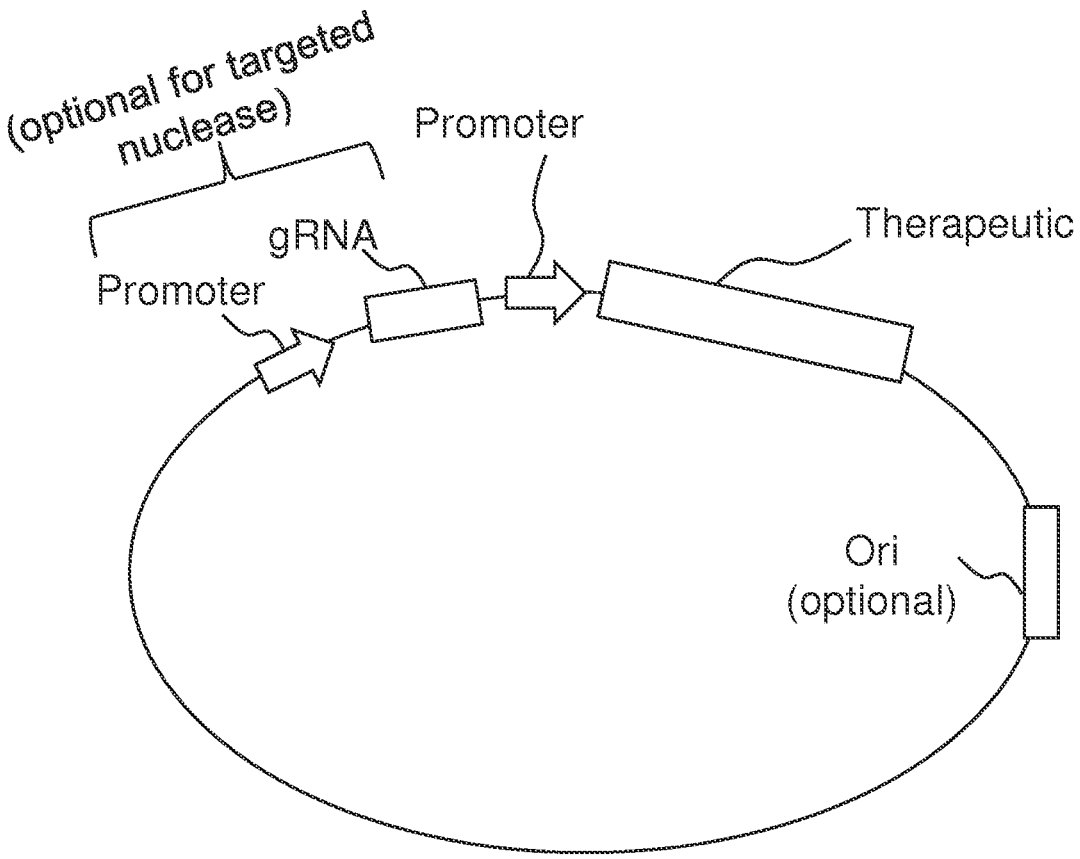

(optional for targeted nuclease)
Promoter
gRNA
Therapeutic
Promoter
Ori
(optional)

FIG. 12