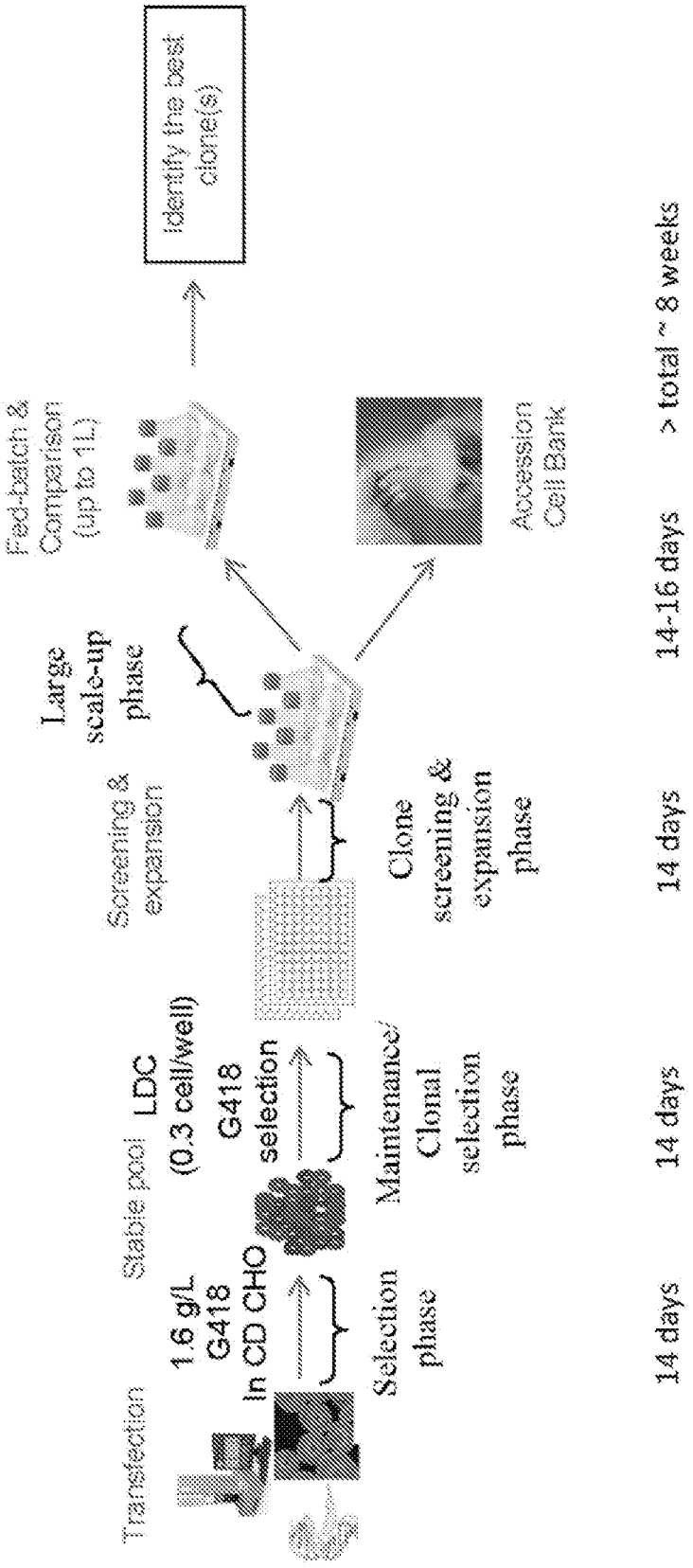

Transfection
1.6 g/L G418 In CD CHO
Selection phase
14 days
Stable pool
LDC (0.3 cell/well)
G418 selection
Maintenance/ Clonal selection phase
14 days
Screening & expansion
Clone screening & expansion phase
14 days
Large scale-up phase
Fed-batch & Comparison (up to 1L)
14-16 days
Accession Cell Bank
Identify the best clone(s)
> total ~ 8 weeks

FIG. 1

FIG. 2A

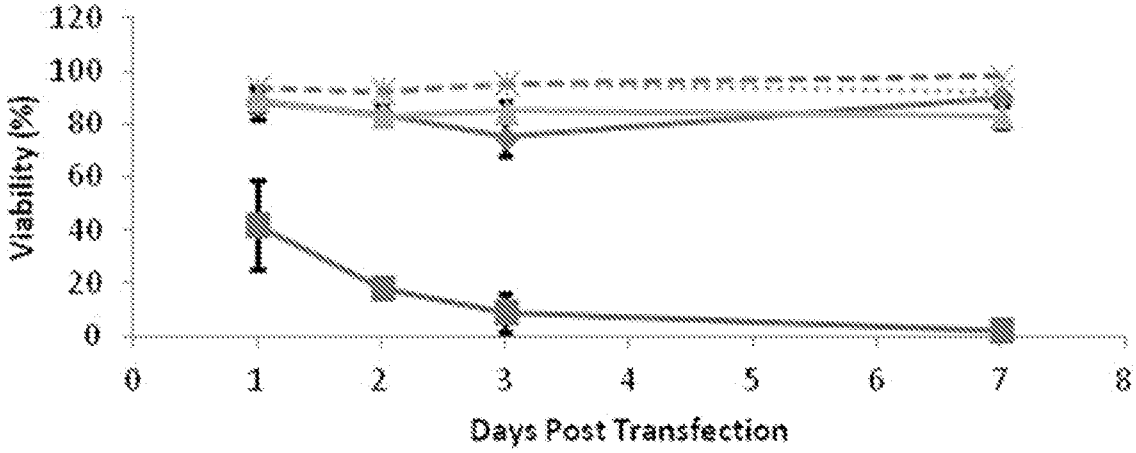


FIG. 2B

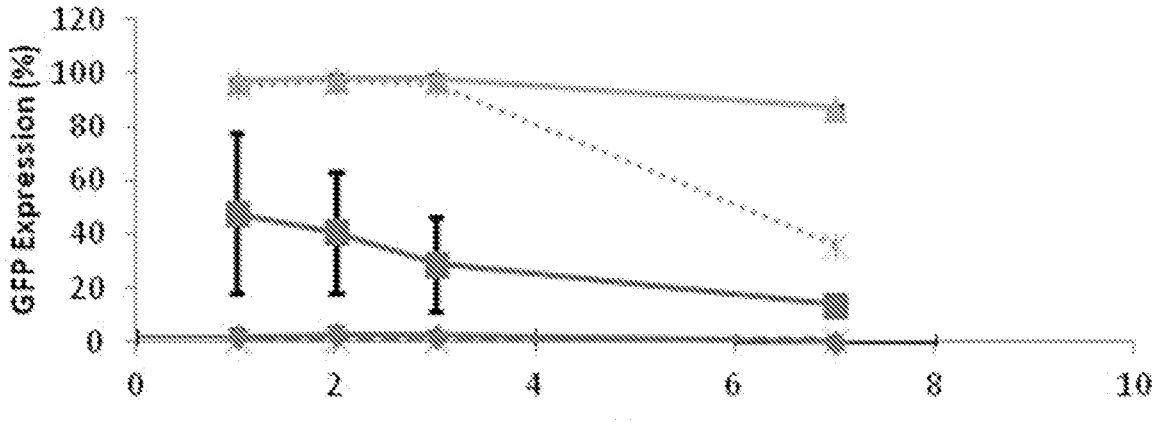
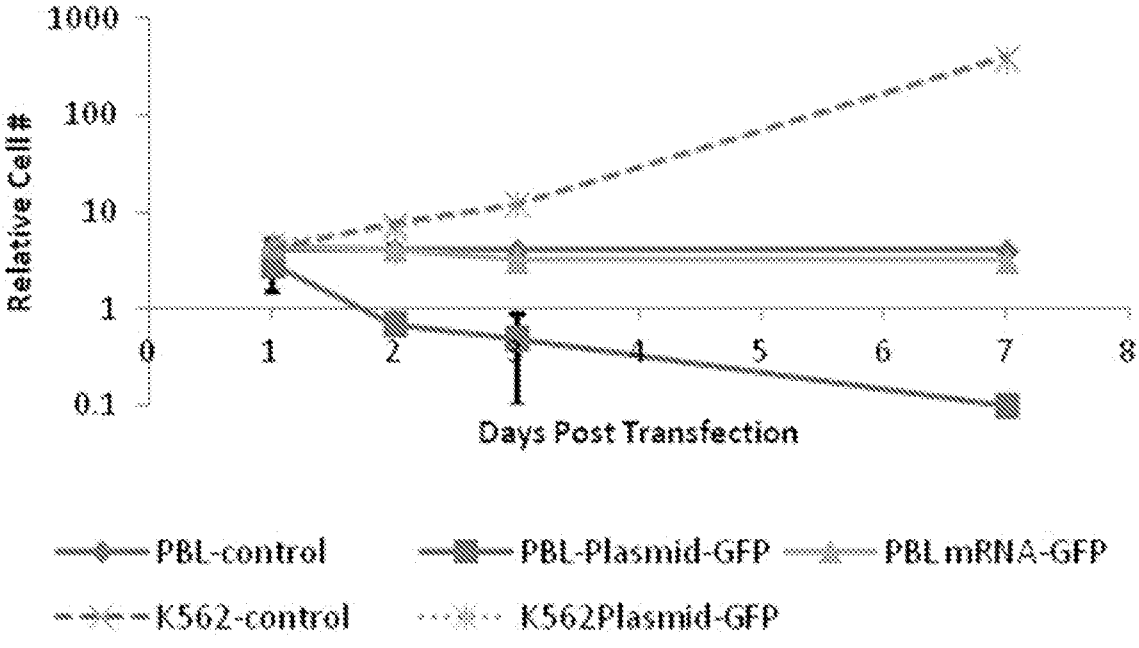


FIG. 2C



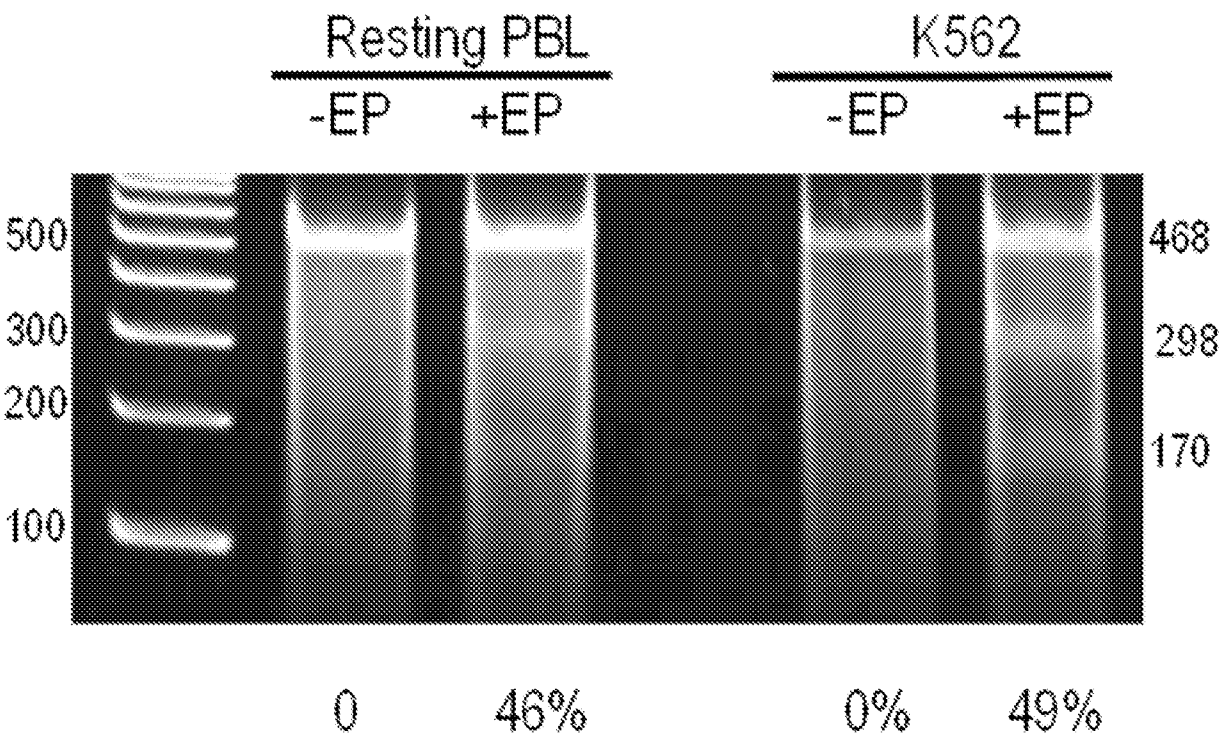

Resting PBL
K562
-EP
+EP
-EP
+EP
500
300
200
100
468
298
170
0
46%
0%
49%

FIG. 3

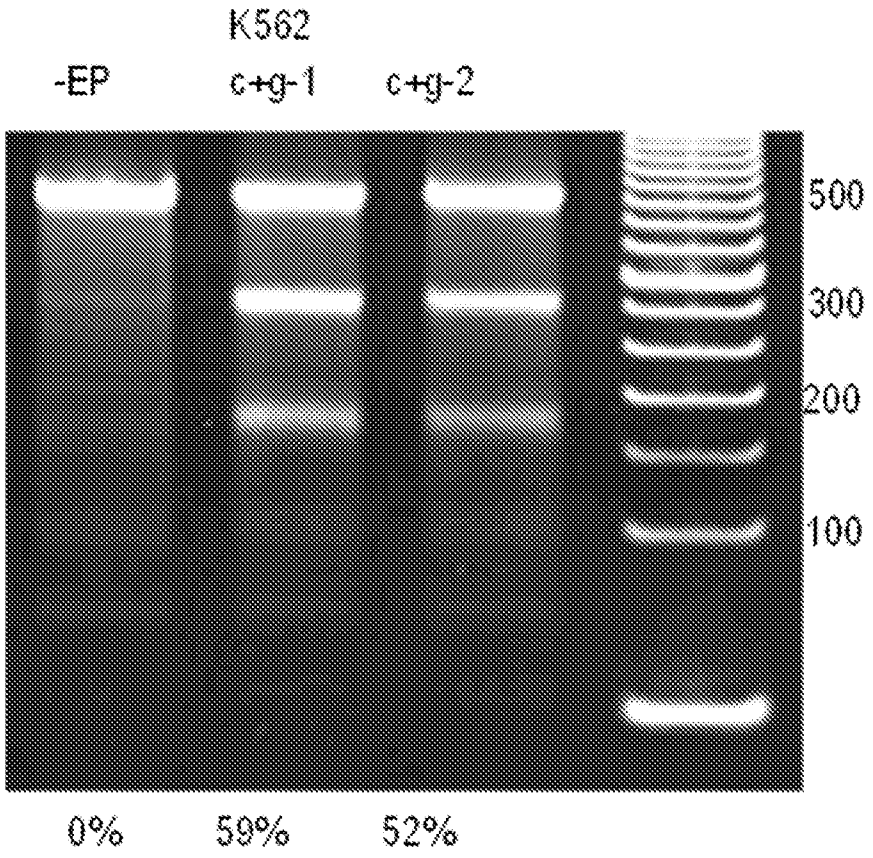

K562
-EP
c+g-1
c+g-2
500
300
200
100
0%
59%
52%

FIG. 4

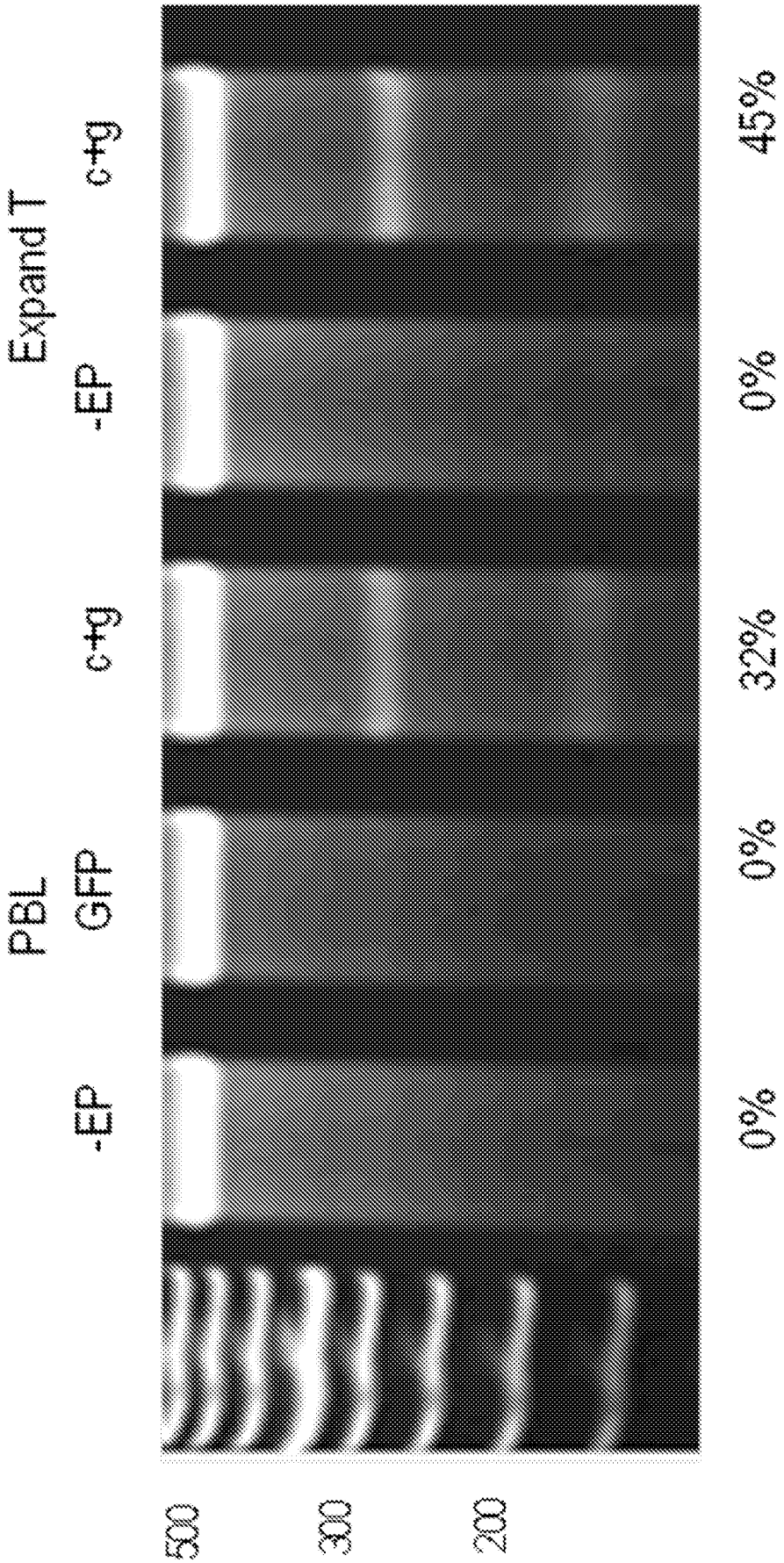


FIG. 5

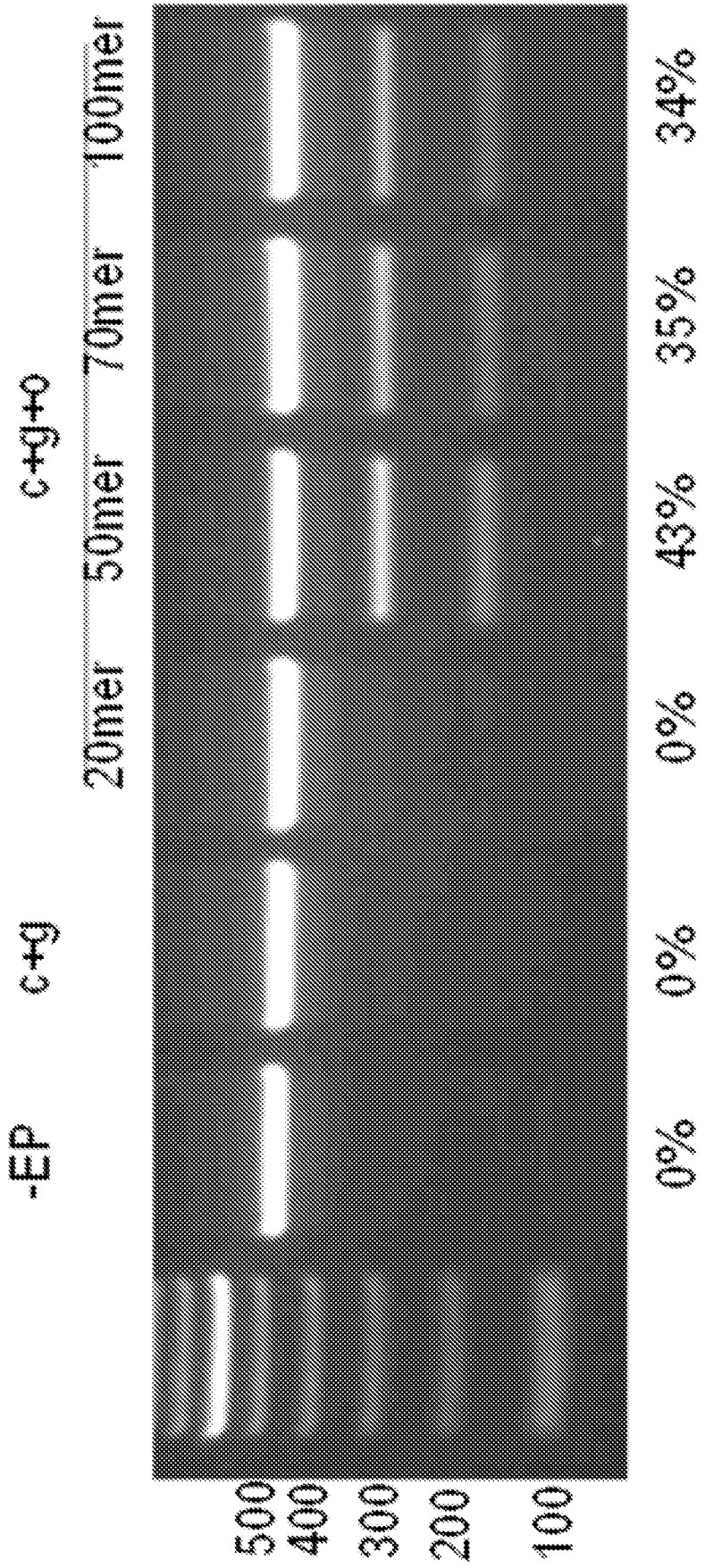

-EP
c+g
c+g+o
20mer
50mer
70mer
100mer
0%
0%
0%
43%
35%
34%
500
400
300
200
100

FIG. 6

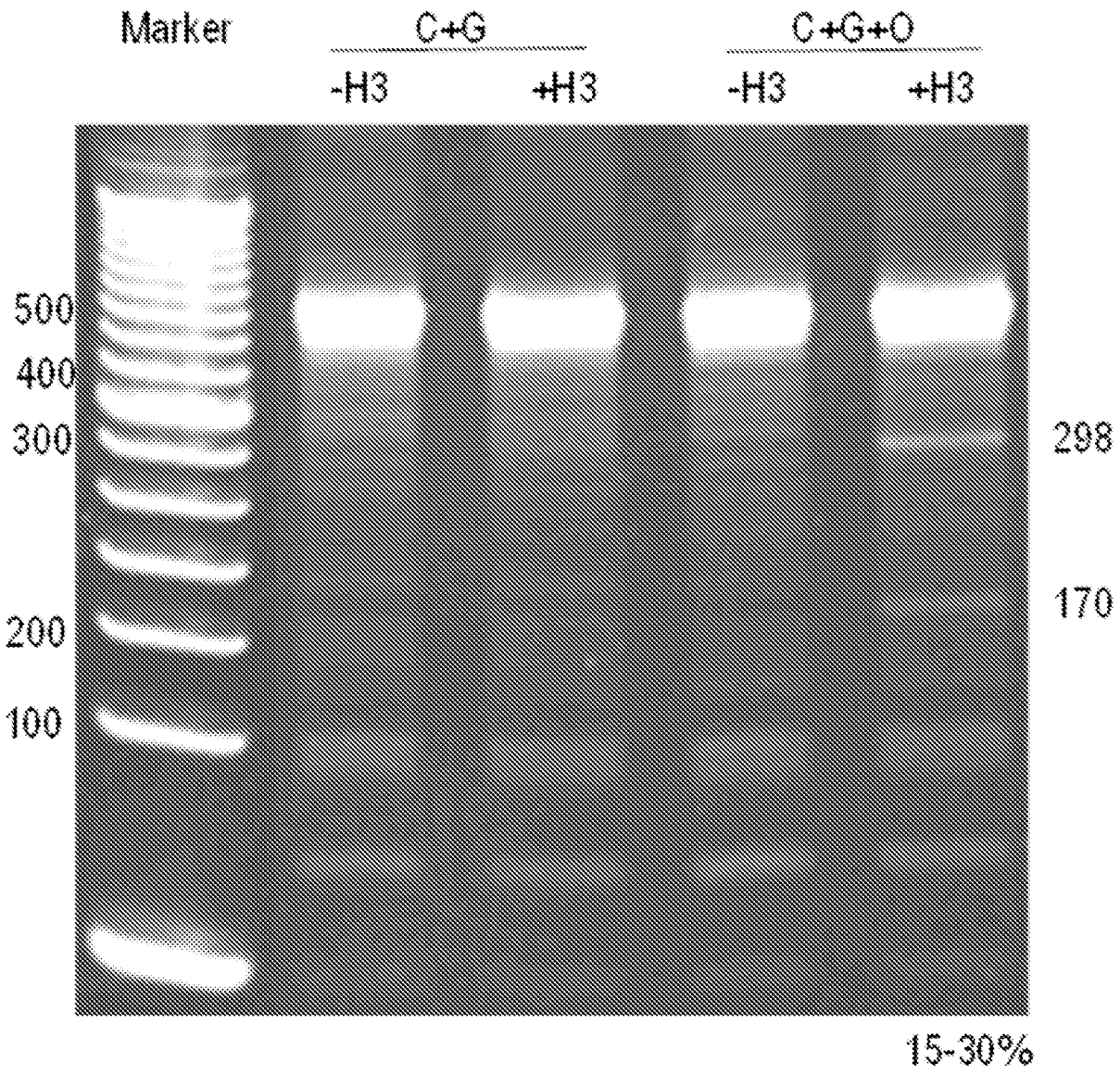


FIG. 7

FIG. 8A

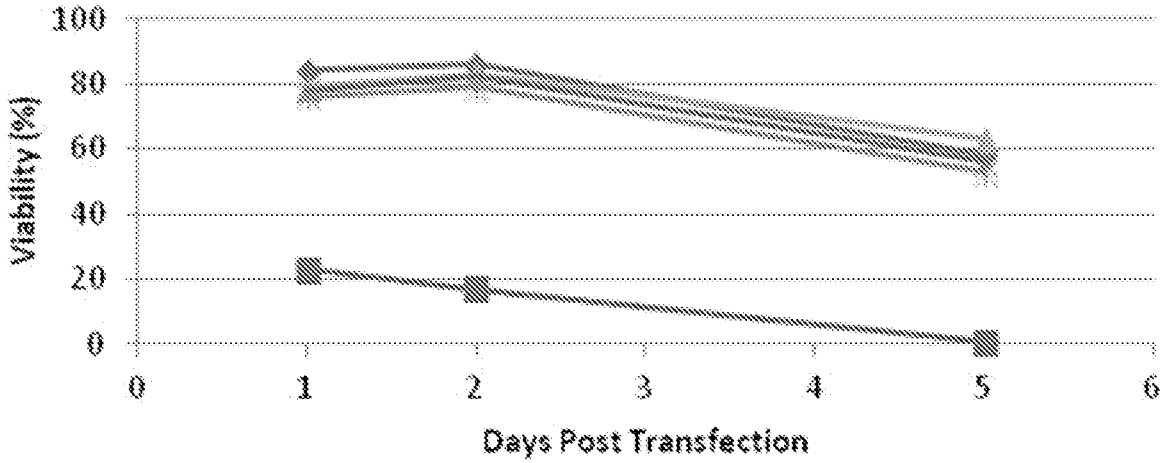


FIG. 8B

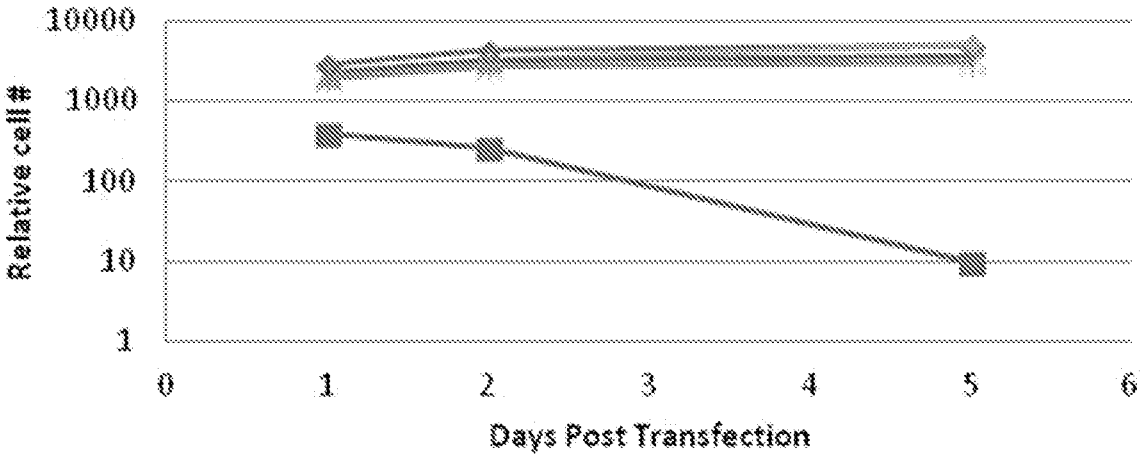
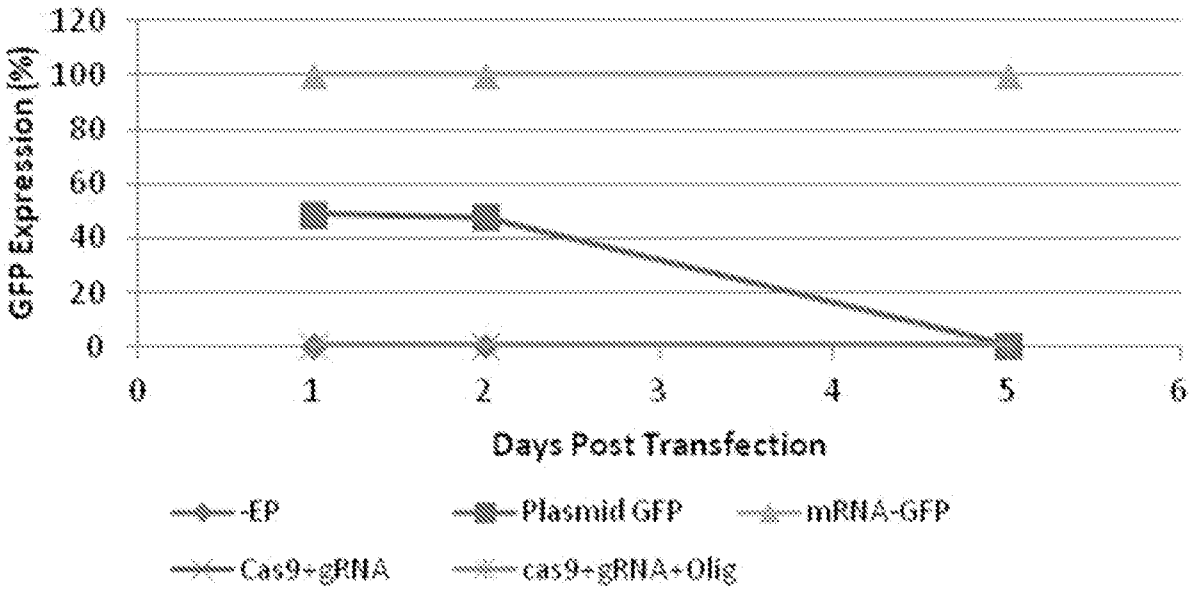


FIG. 8C



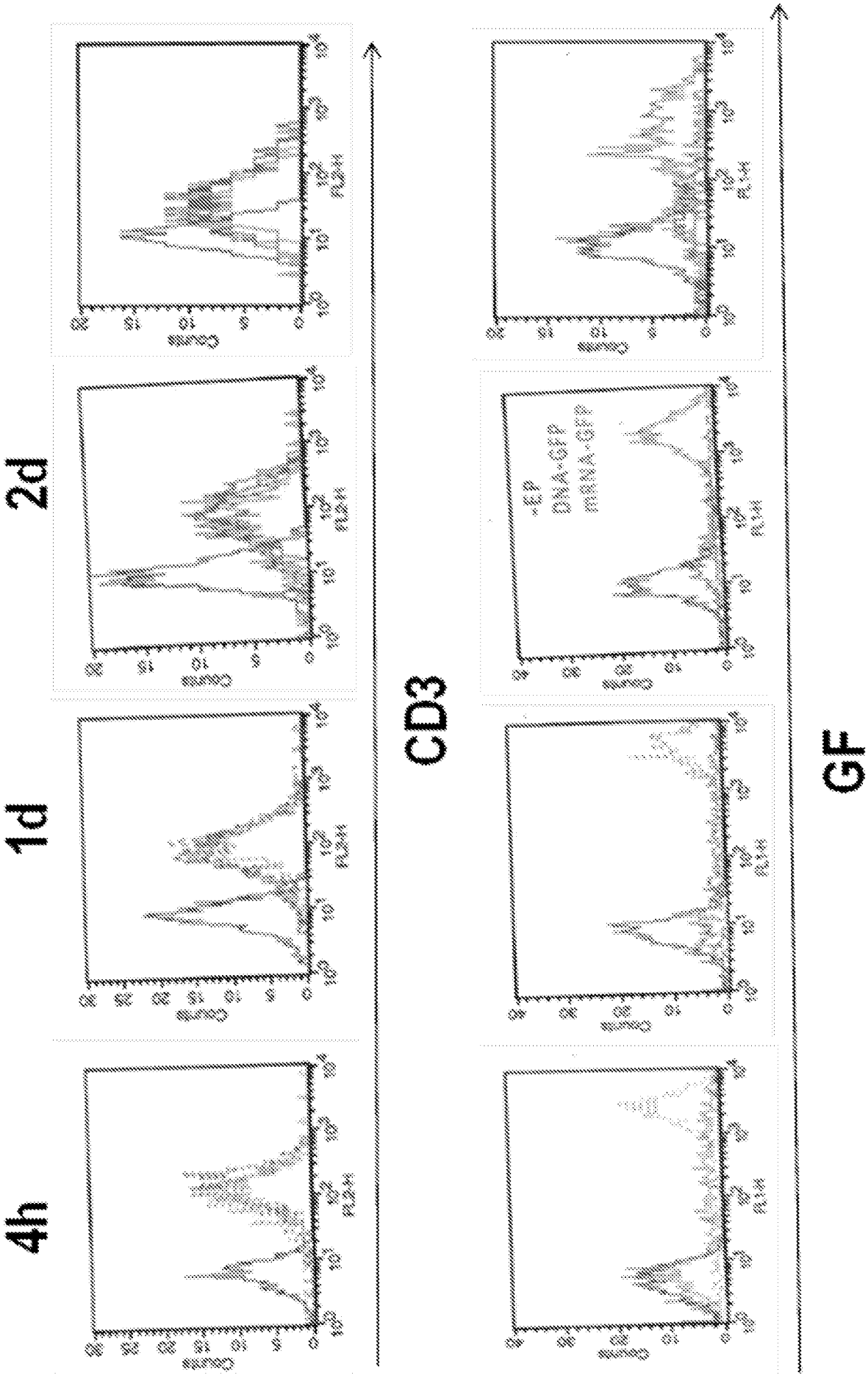


FIG. 9

FIG. 10A

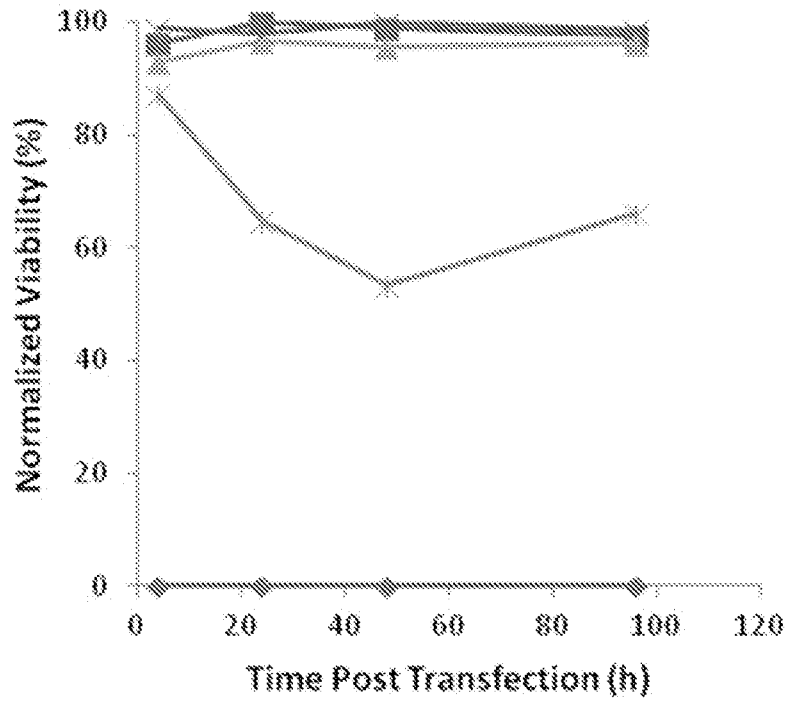


FIG. 10B

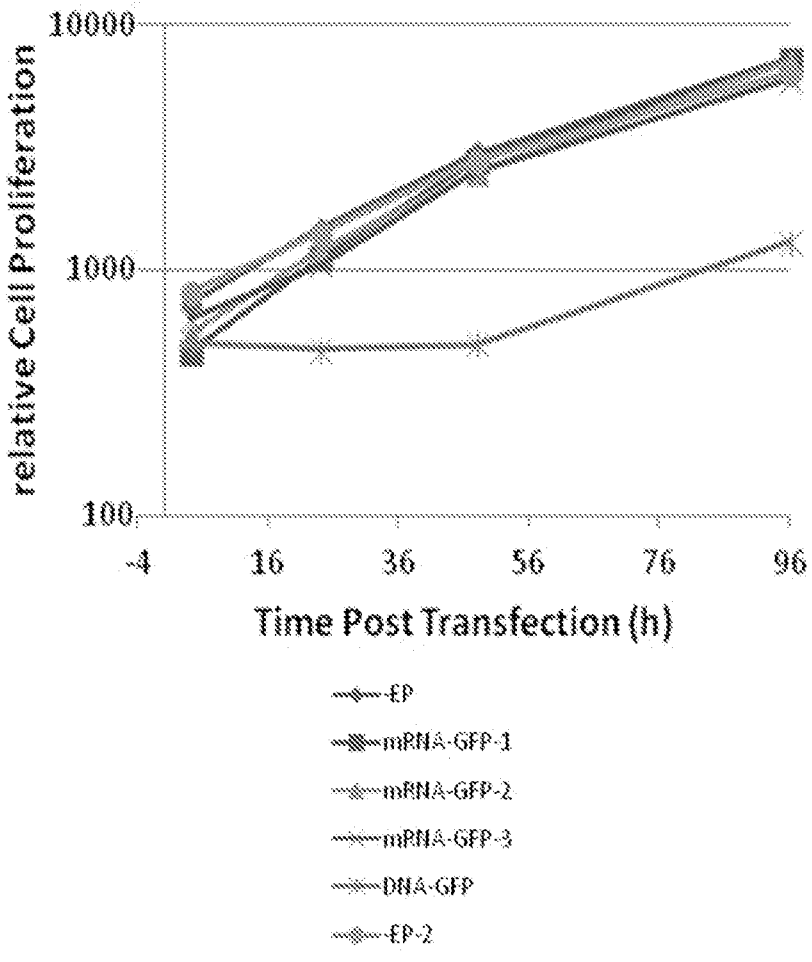


FIG.10C

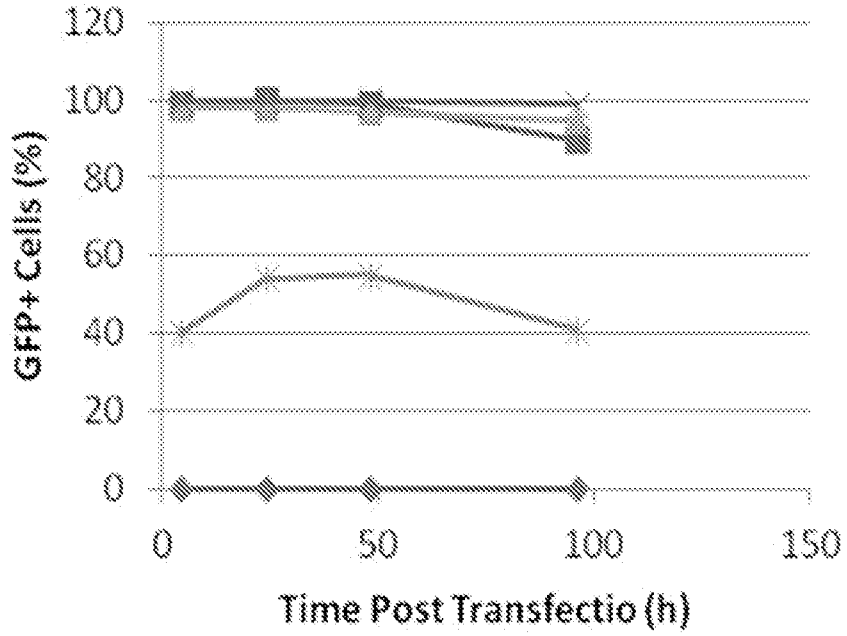


FIG. 10D

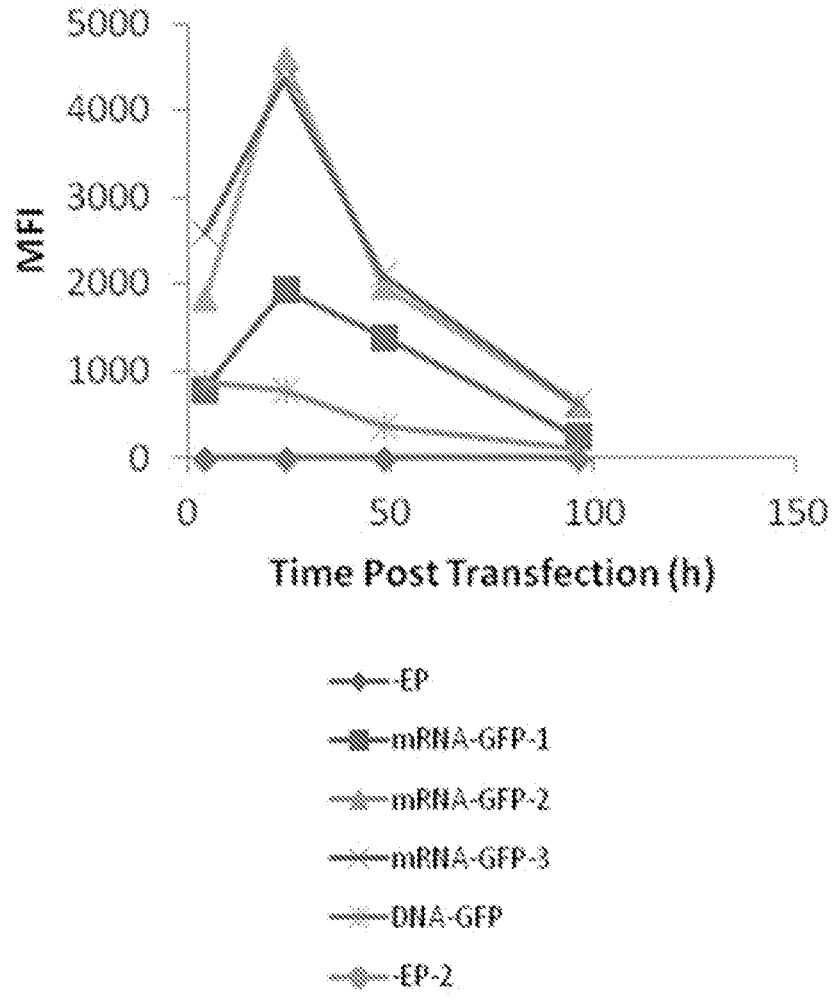


FIG. 11A

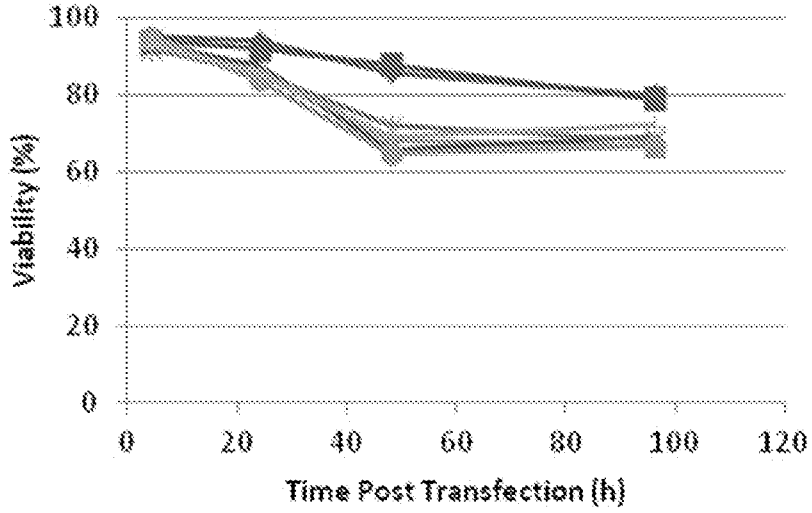


FIG. 11B

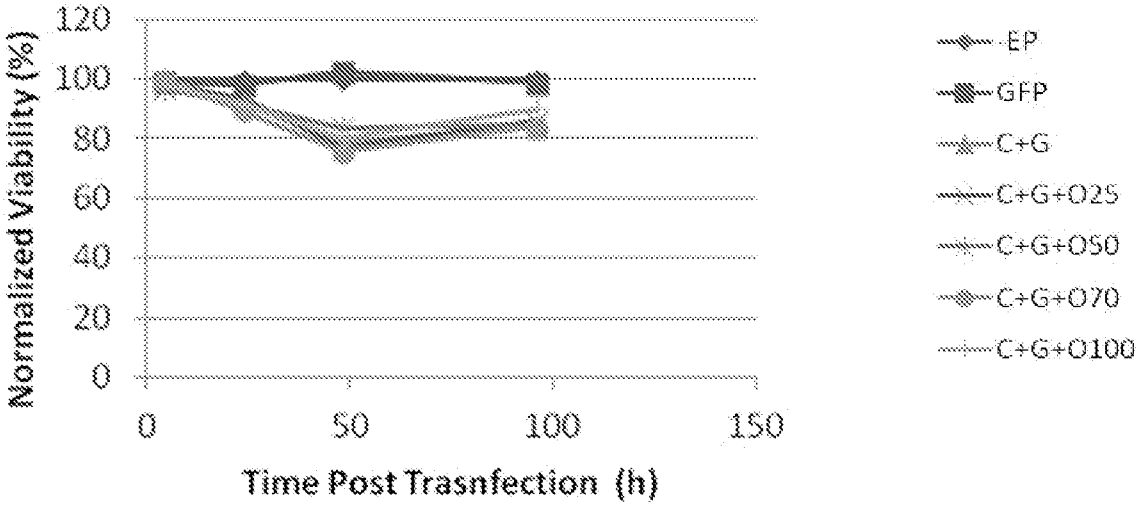
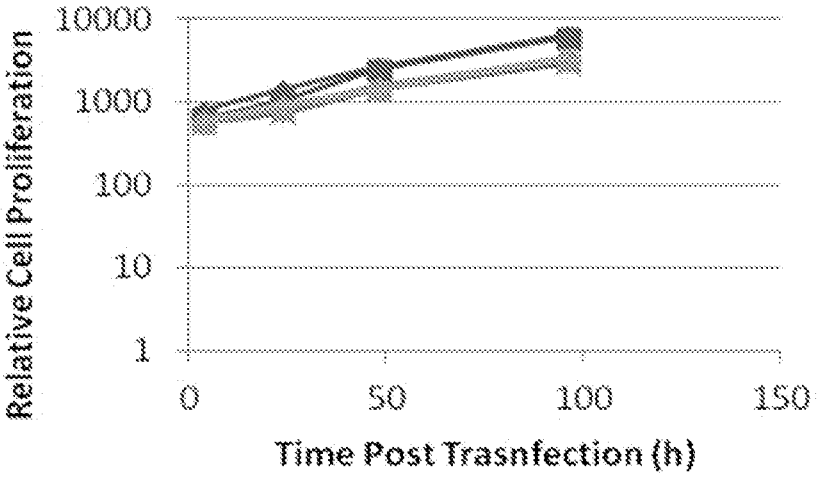


FIG. 11C



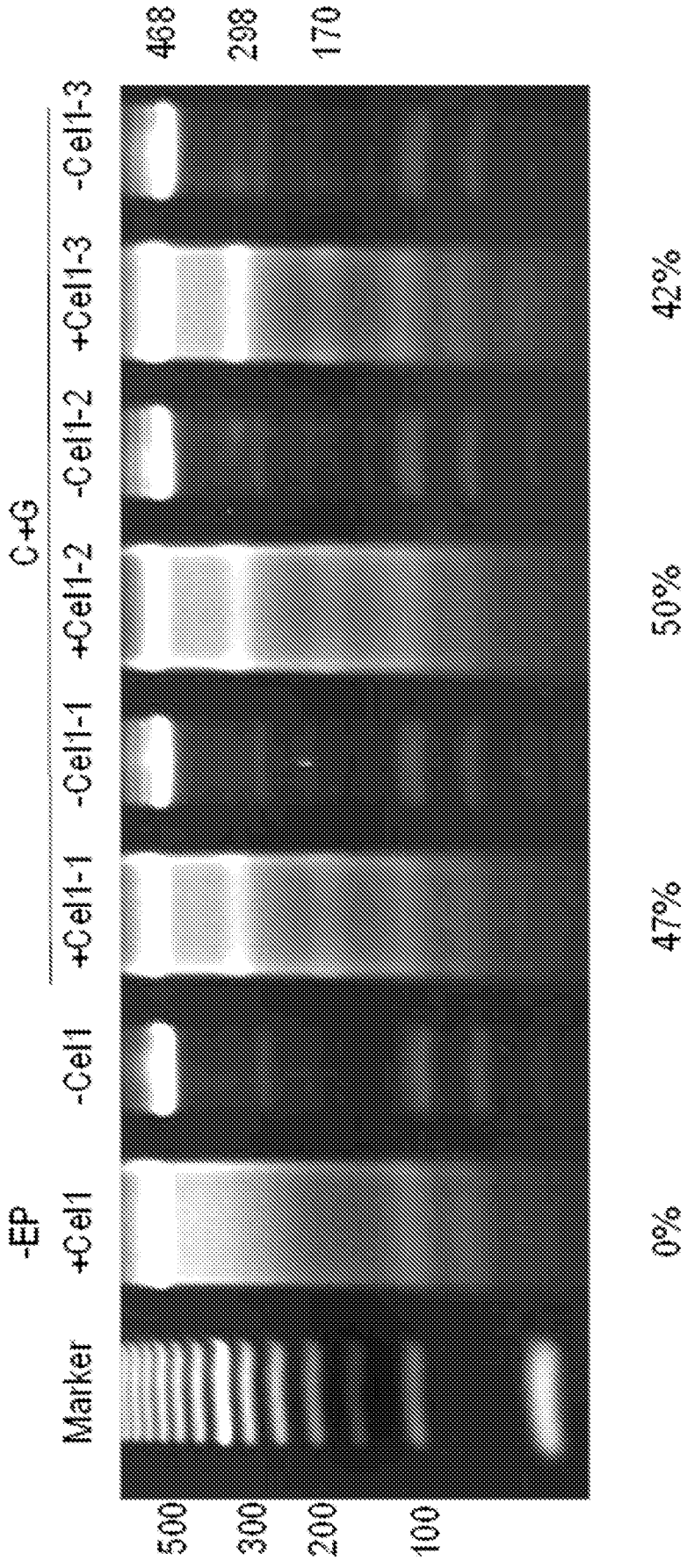

468
298
170
C+G
-EP
+Cel1
-Cel1
+Cel1-1
-Cel1-1
+Cel1-2
-Cel1-2
+Cel1-3
-Cel1-3
Marker
0%
47%
50%
42%
500
300
200
100

FIG. 12

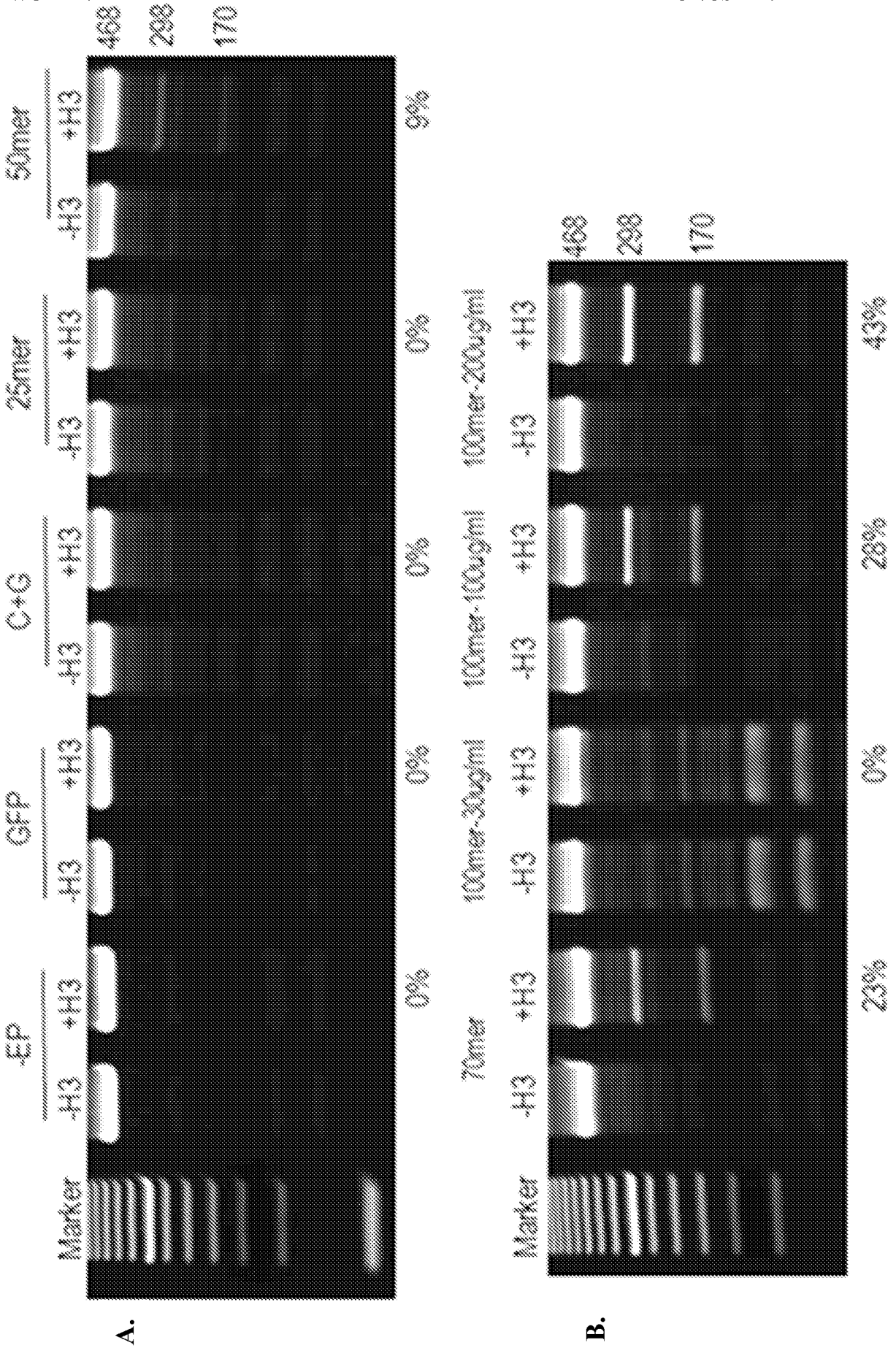

468
288
170
50mer
-H3
+H3
6%
26mer
0%
C+G
0%
GFP
0%
EP
0%
Marker
A.
468
288
170
100mer-200ug/ml
43%
100mer-100ug/ml
28%
100mer-30ug/ml
0%
70mer
23%
Marker
B.

FIG. 13A-13B

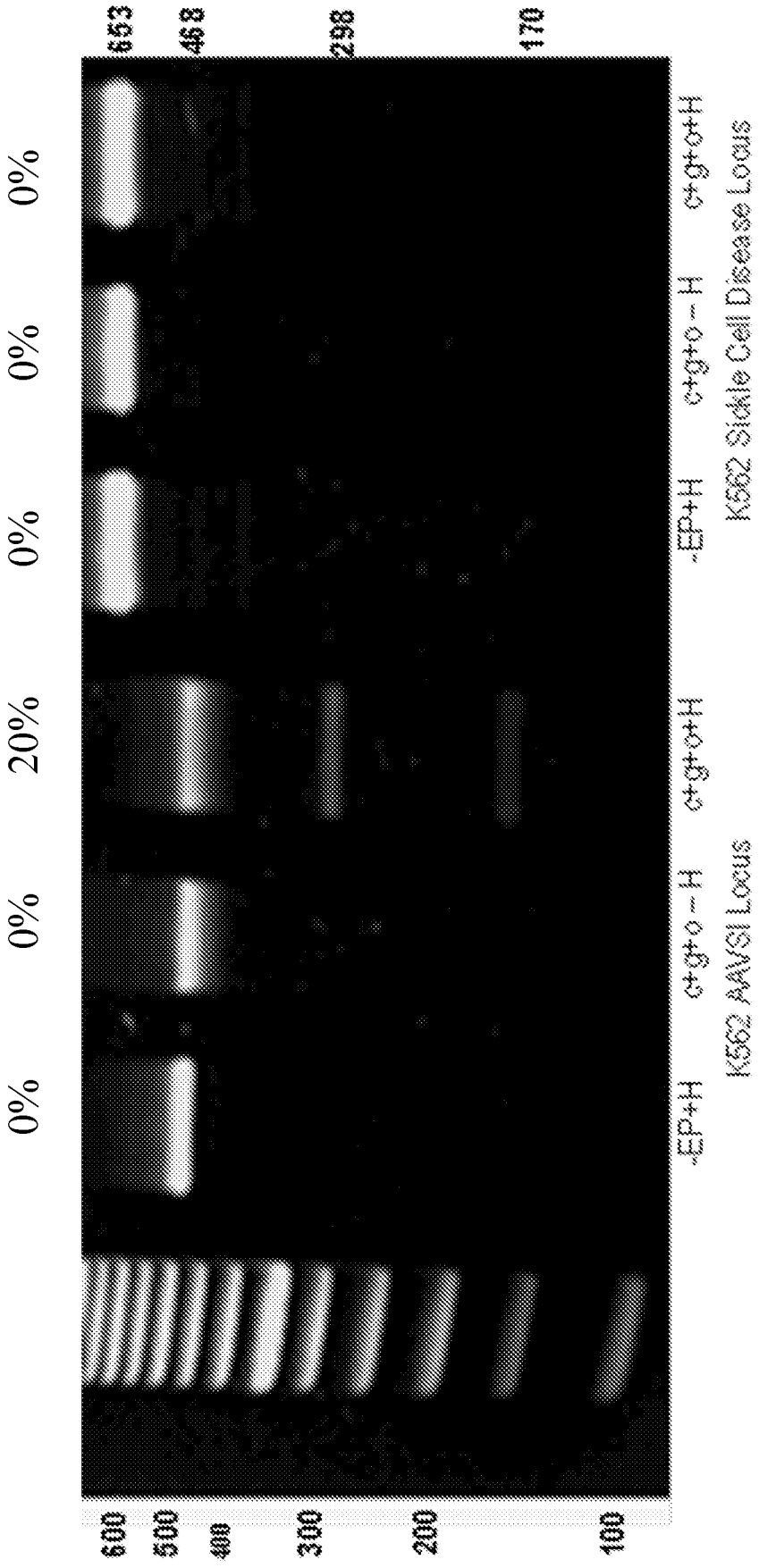

653
468
298
170
600
500
400
300
200
100
0%
0%
0%
20%
0%
0%
-EP+H
c+g+o-H
c+g+o+H
K562 AAVSI Locus
-EP+H
c+g+o-H
c+g+o+H
K562 Sickle Cell Disease Locus

FIG. 14

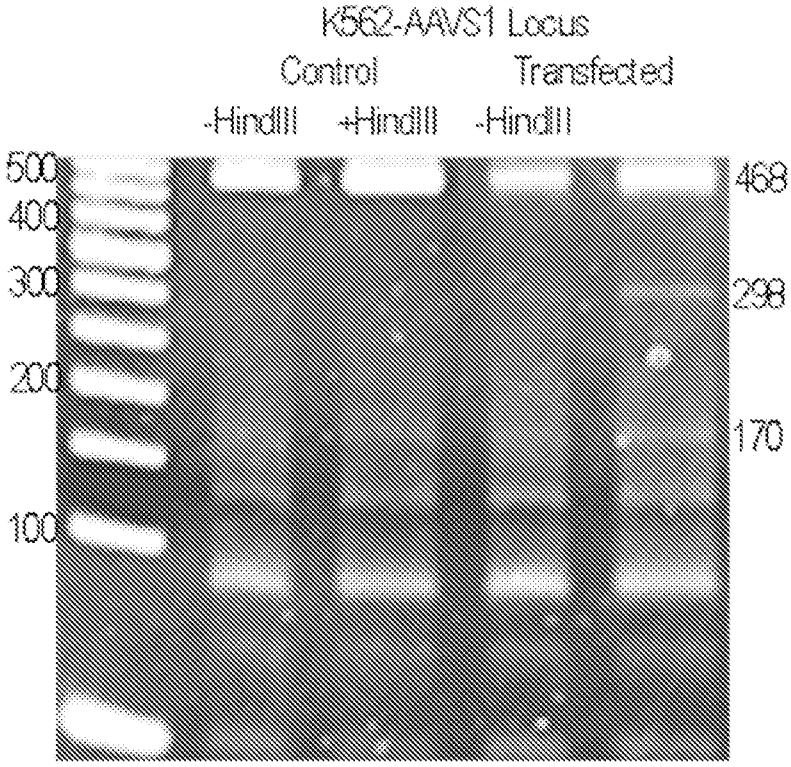


FIG. 15A

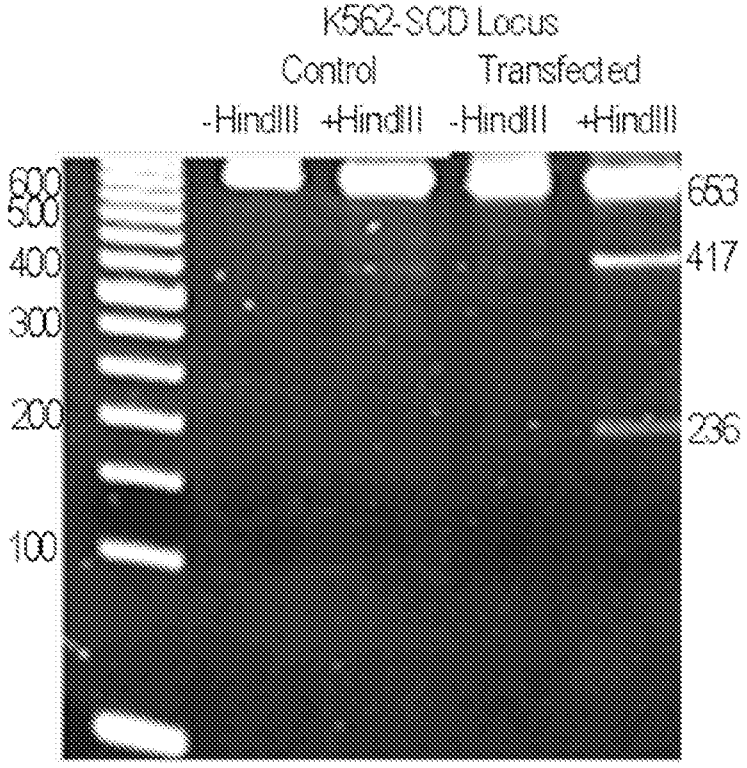


FIG. 15B

Donor DNA: atggtgcatctgactcctgTAGtggagaagtctgccgttact

Target genomic DNA:
atggtgcatctgactcctgtggagaagtctgccgttact
taccacgtagactgaggacacctcttcagacggcaatga

FIG. 16A

Donor DNA: atggtgcatctgactcctgAggagaagtctgccgttact

Target genomic DNA:
atggtgcatctgactcctgtggagaagtctgccgttact
taccacgtagactgaggacacctcttcagacggcaatga

FIG. 16B

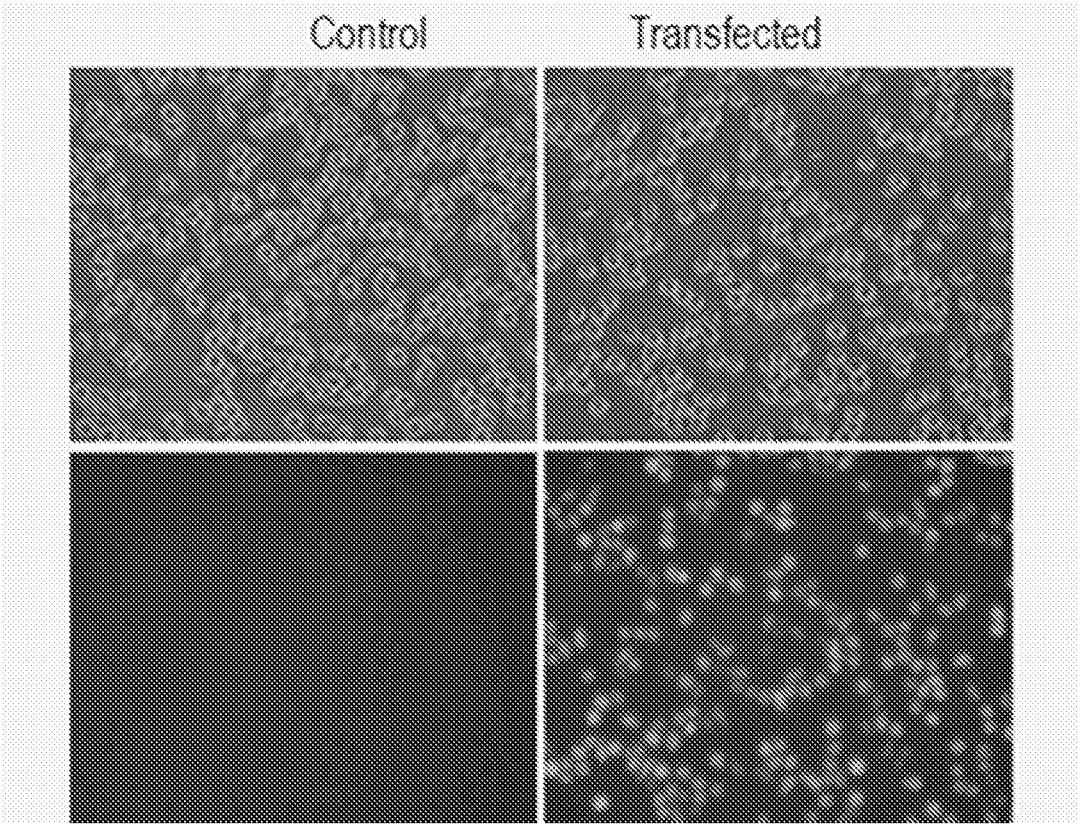

Control
Transfected

FIG. 17

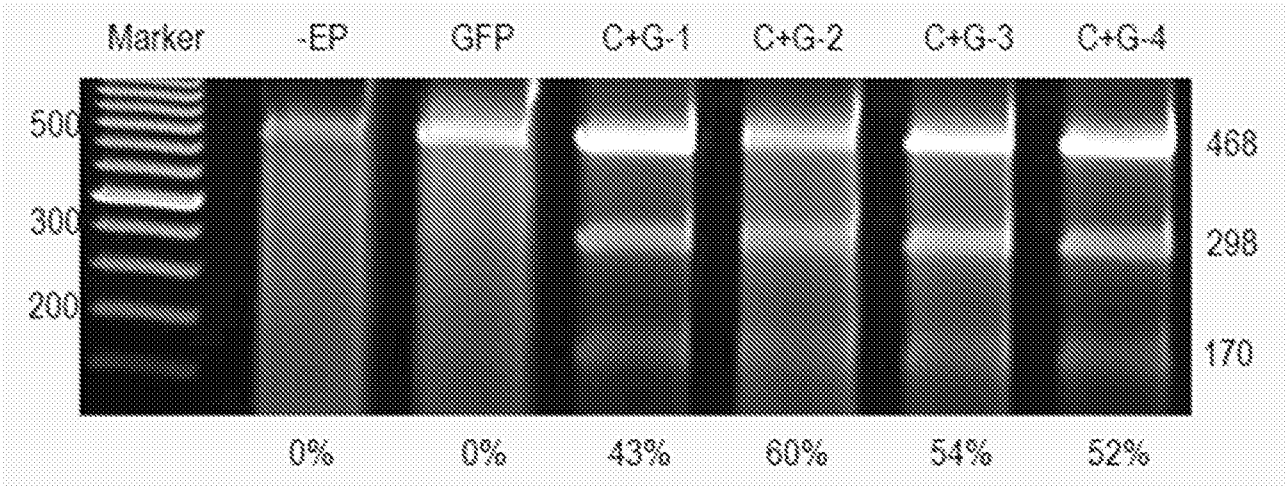

Marker
-EP
GFP
C+G-1
C+G-2
C+G-3
C+G-4
500
300
200
468
298
170
0%
0%
43%
60%
54%
52%

FIG. 18

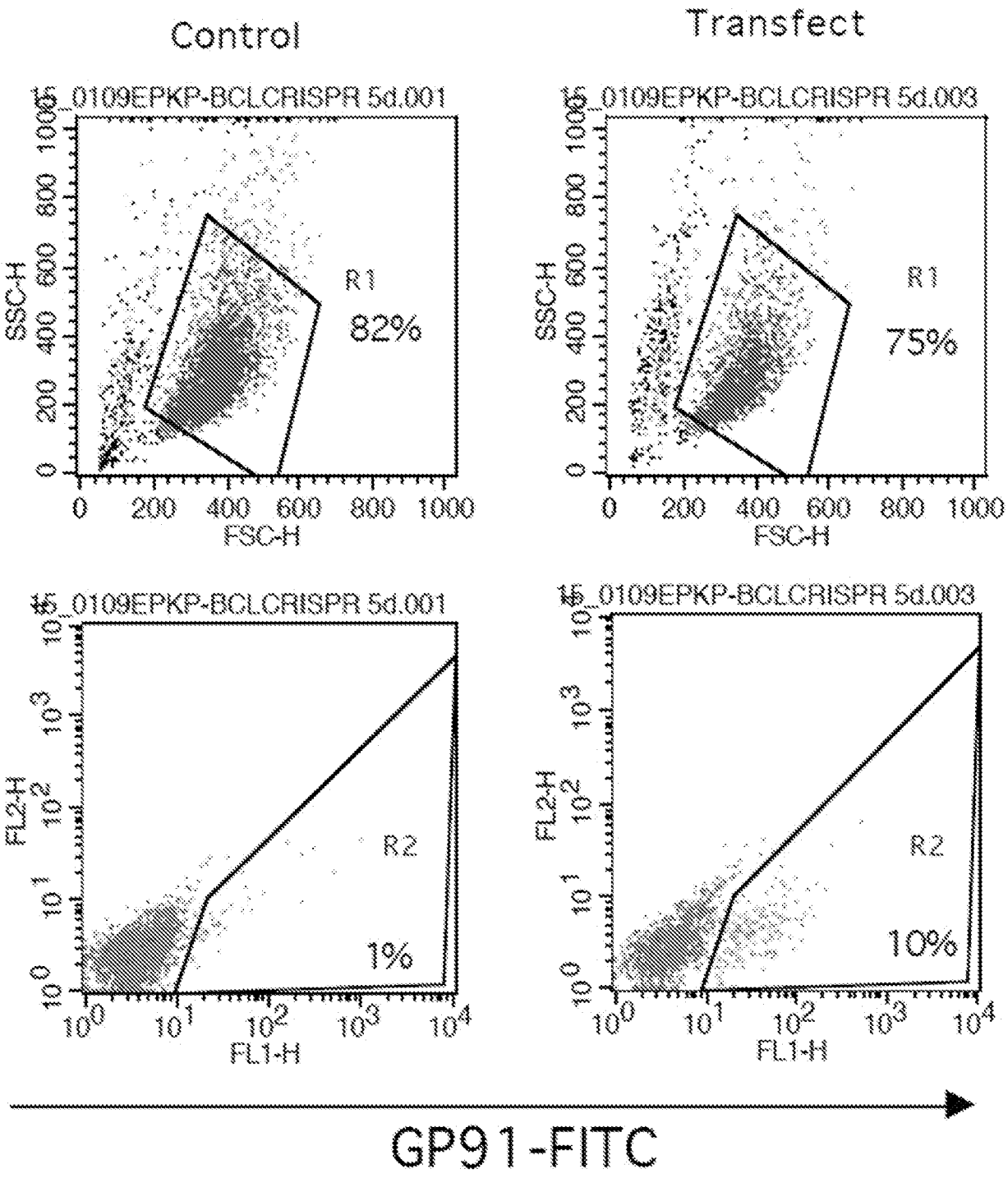

Control
Transfect
15_0109EPKP-BCLCRISPR 5d.001
15_0109EPKP-BCLCRISPR 5d.003
SSC-H
FSC-H
R1
82%
75%
FL2-H
FL1-H
R2
1%
10%
GP91-FITC

FIG. 19