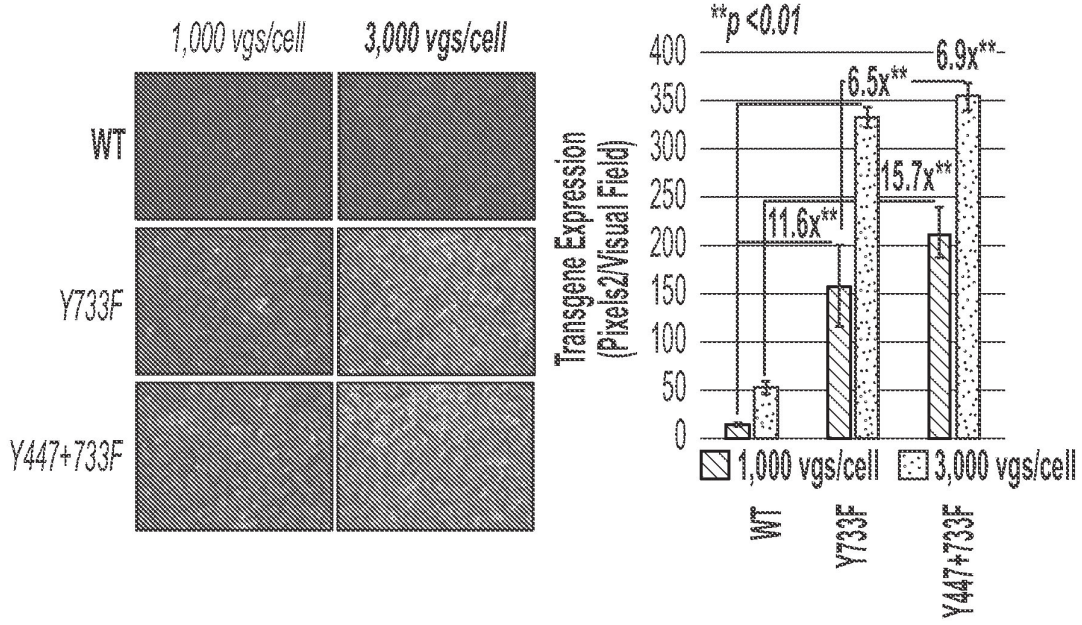

1,000 vgs/cell
3,000 vgs/cell
WT
Y733F
Y447+733F
**p <0.01
Transgene Expression
(Pixels2/Visual Field)
400
350
300
250
200
150
100
50
0
11.6x**
6.5x**
15.7x**
6.9x**
1,000 vgs/cell
3,000 vgs/cell
WT
Y733F
Y447+733F

FIG. 1A

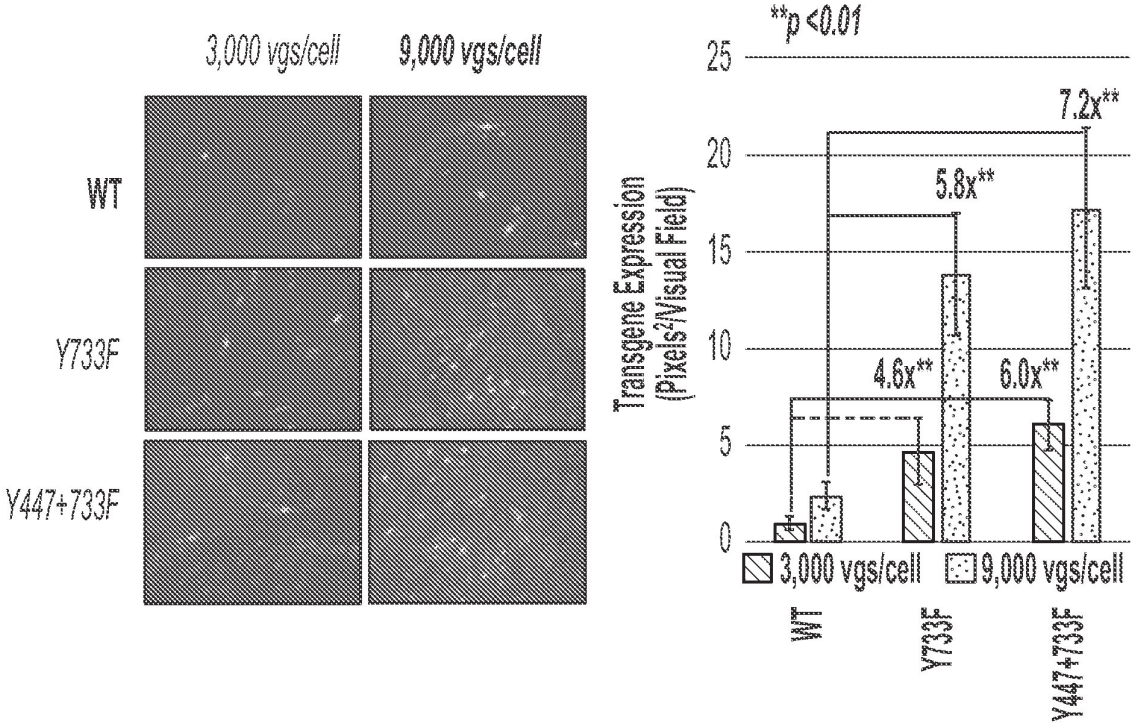

3,000 vgs/cell
9,000 vgs/cell
WT
Y733F
Y447+733F
**p <0.01
Transgene Expression
(Pixels2/Visual Field)
25
20
15
10
5
0
4.6x**
5.8x**
6.0x**
7.2x**
3,000 vgs/cell
9,000 vgs/cell
WT
Y733F
Y447+733F

FIG. 1B

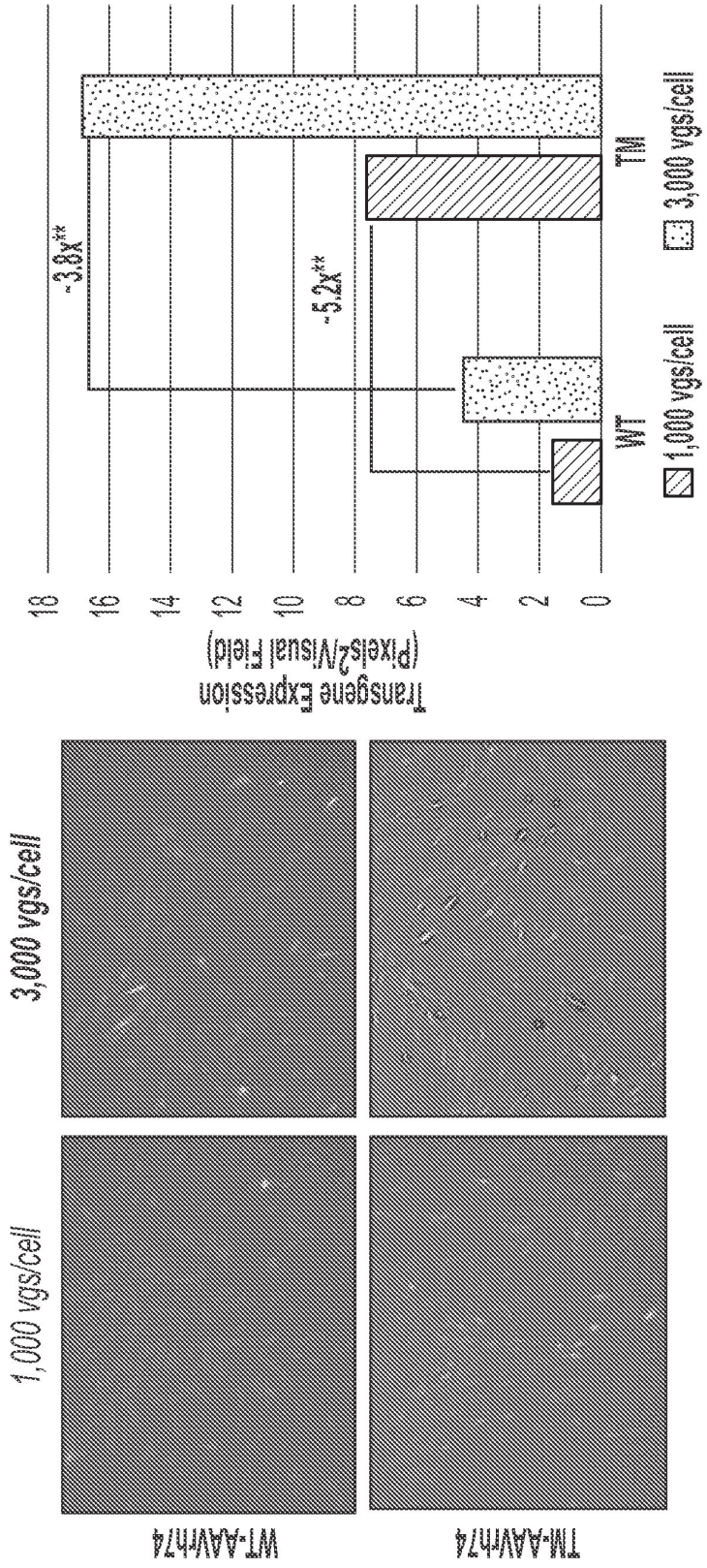

Transgene Expression
(Pixels^2/Visual Field)
18
16
14
12
10
8
6
4
2
0
~3.8x**
~5.2x**
WT
TM
1,000 vgs/cell
3,000 vgs/cell
3,000 vgs/cell
1,000 vgs/cell
WT-AAVrh74
TM-AAVrh74

FIG. 2

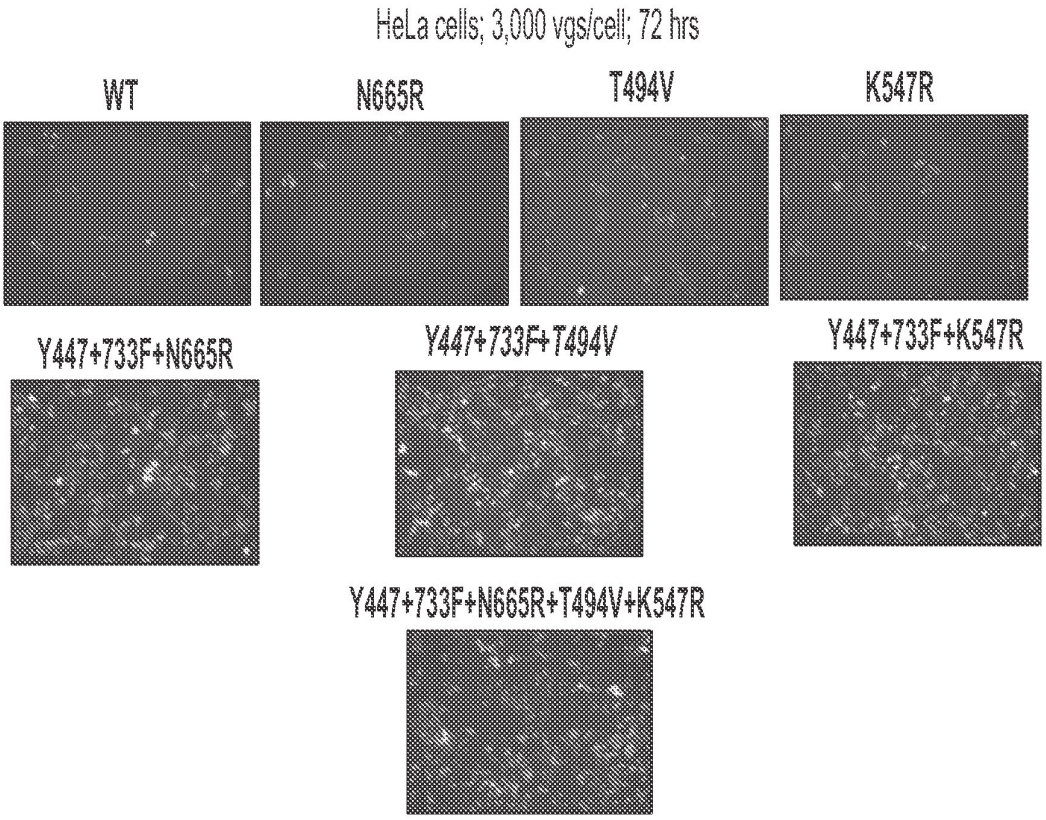

HeLa cells; 3,000 vgs/cell; 72 hrs
WT
N665R
T494V
K547R
Y447+733F+N665R
Y447+733F+T494V
Y447+733F+K547R
Y447+733F+N665R+T494V+K547R

FIG. 3A

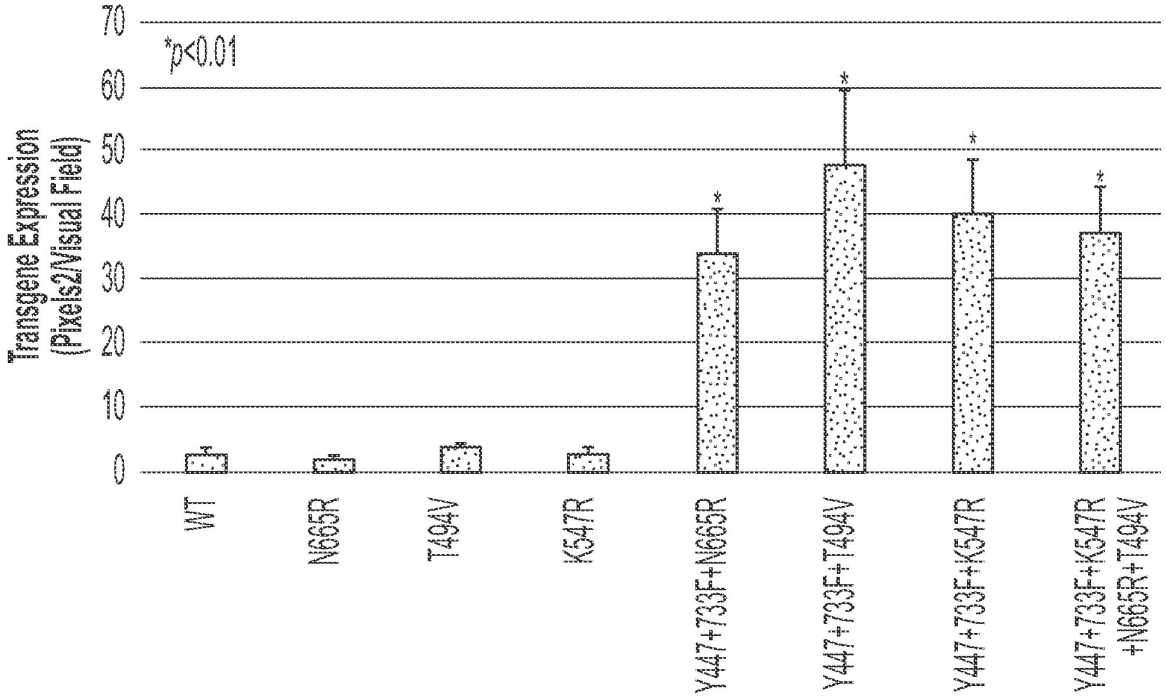

Transgene Expression
(Pixels2/Visual Field)
70
60
50
40
30
20
10
0
*p<0.01
*
*
*
*
WT
N665R
T494V
K547R
Y447+733F+N665R
Y447+733F+T494V
Y447+733F+K547R
Y447+733F+K547R
+N665R+T494V

FIG. 3B

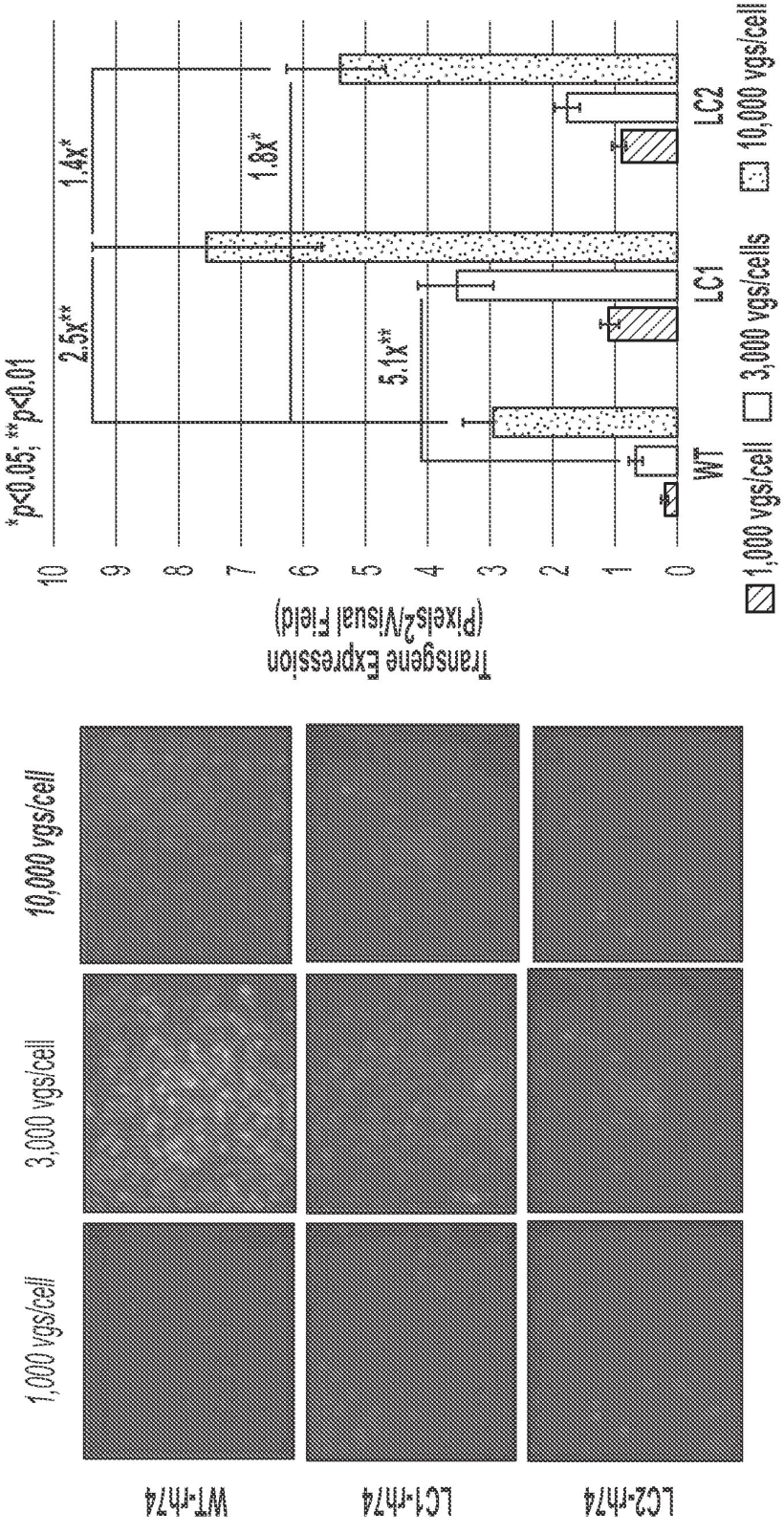

WT-rh74
LC1-rh74
LC2-rh74
1,000 vgs/cell
3,000 vgs/cell
10,000 vgs/cell
Transgene Expression
(Pixels^2/Visual Field)
*p<0.05; **p<0.01
2.5x**
5.1x**
1.4x*
1.8x*
WT
LC1
LC2
1,000 vgs/cell
3,000 vgs/cells
10,000 vgs/cell

FIG. 4A

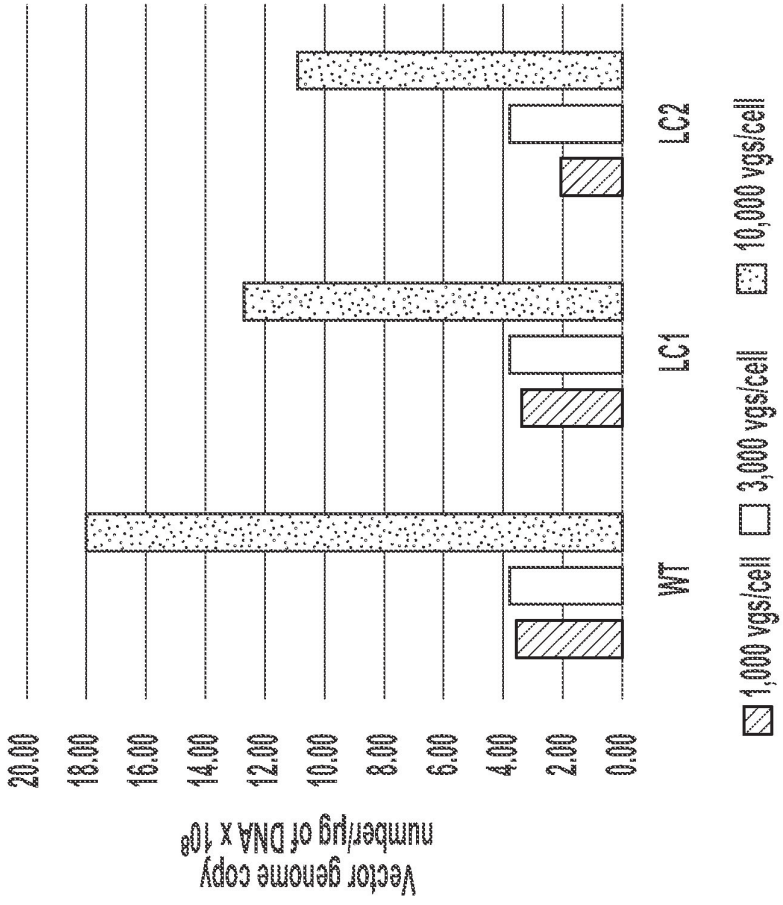

Vector genome copy number/µg of DNA x 10^8
20.00
18.00
16.00
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
WT
LC1
LC2
1,000 vgs/cell
3,000 vgs/cell
10,000 vgs/cell

FIG. 4B

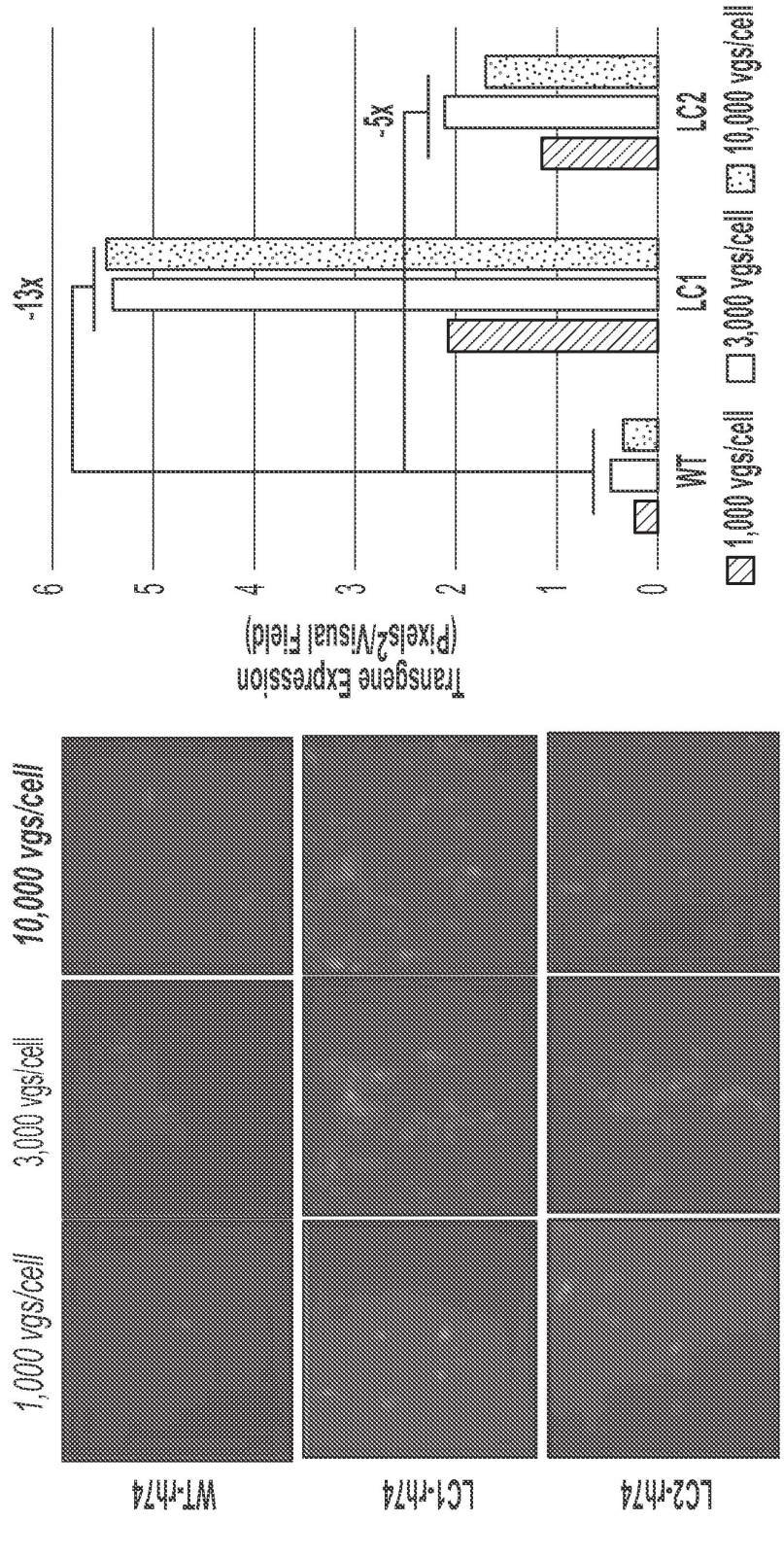
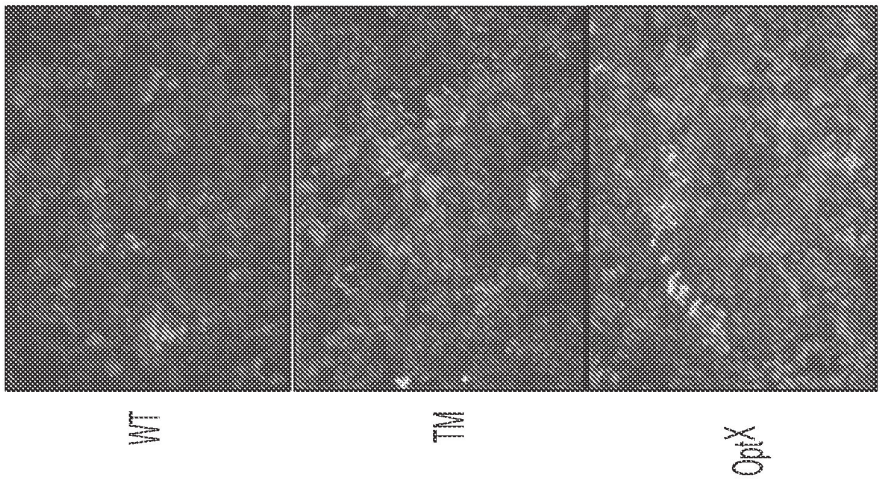

1,000 vgs/cell
3,000 vgs/cell
10,000 vgs/cell
WT-rh74
LC1-rh74
LC2-rh74
Transgene Expression
(Pixels^2/Visual Field)
6
5
4
3
2
1
0
-13x
-5x
WT
LC1
LC2
1,000 vgs/cell
3,000 vgs/cell
10,000 vgs/cell

FIG. 4C


WT
TM
OptX

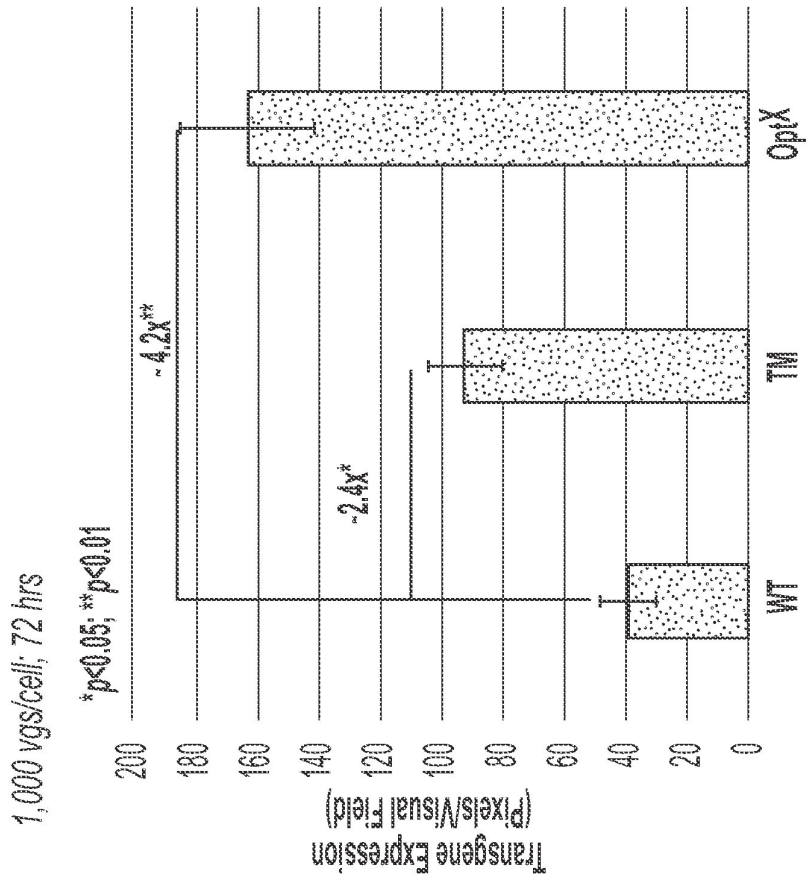

1,000 vgs/cell; 72 hrs
*p<0.05; **p<0.01
~4.2x**
~2.4x*
Transgene Expression
(Pixels/Visual Field)
200
180
160
140
120
100
80
60
40
20
0
WT
TM
OptX

FIG. 5

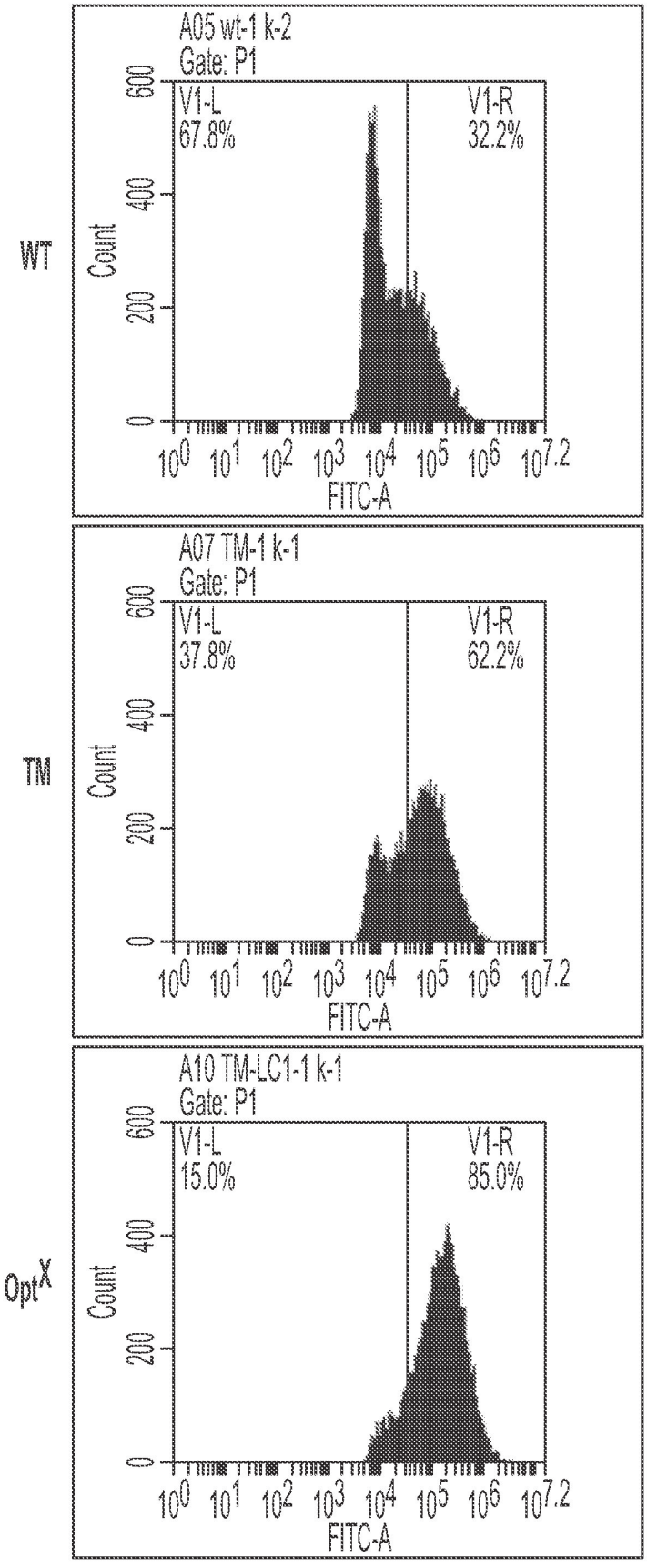

WT
A05 wt-1 k-2
Gate: P1
V1-L
67.8%
V1-R
32.2%
Count
FITC-A
TM
A07 TM-1 k-1
Gate: P1
V1-L
37.8%
V1-R
62.2%
Count
FITC-A
Opt^X
A10 TM-LC1-1 k-1
Gate: P1
V1-L
15.0%
V1-R
85.0%
Count
FITC-A

FIG. 6A

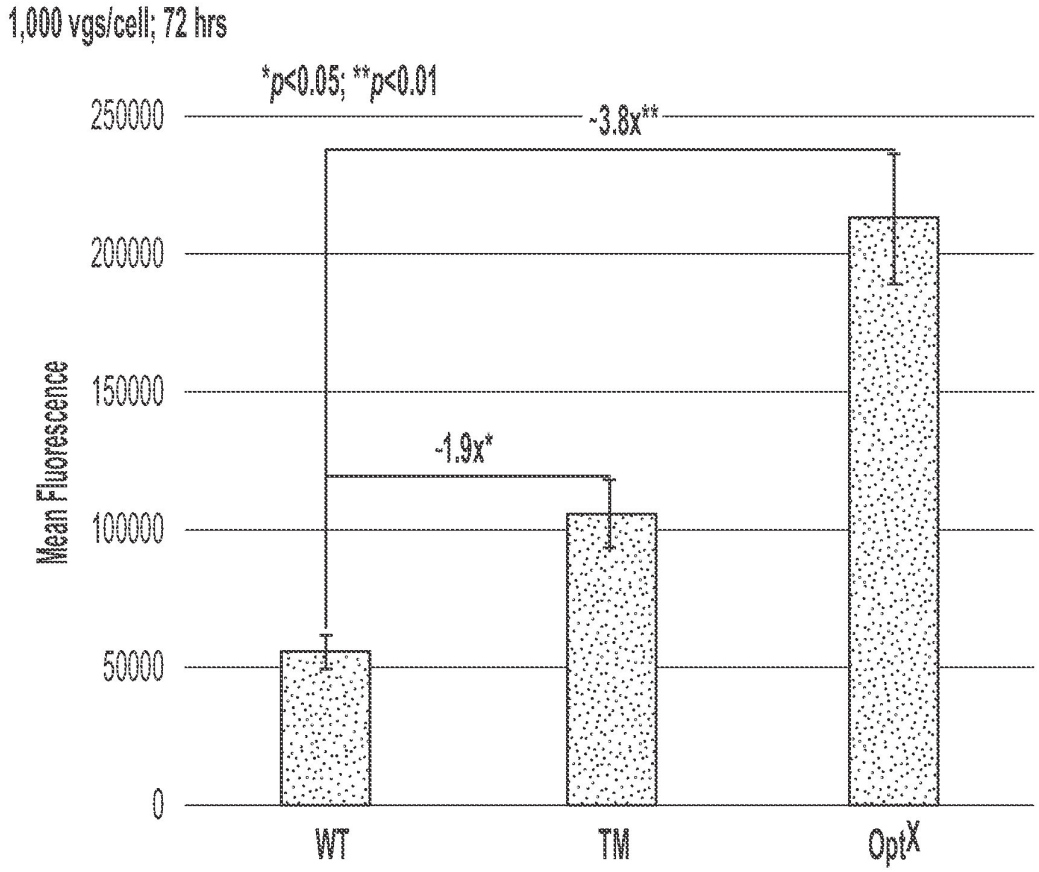

1,000 vgs/cell; 72 hrs
*p<0.05; **p<0.01
250000
200000
150000
100000
50000
0
Mean Fluorescence
~3.8x**
~1.9x*
WT
TM
Opt^X

FIG. 6B

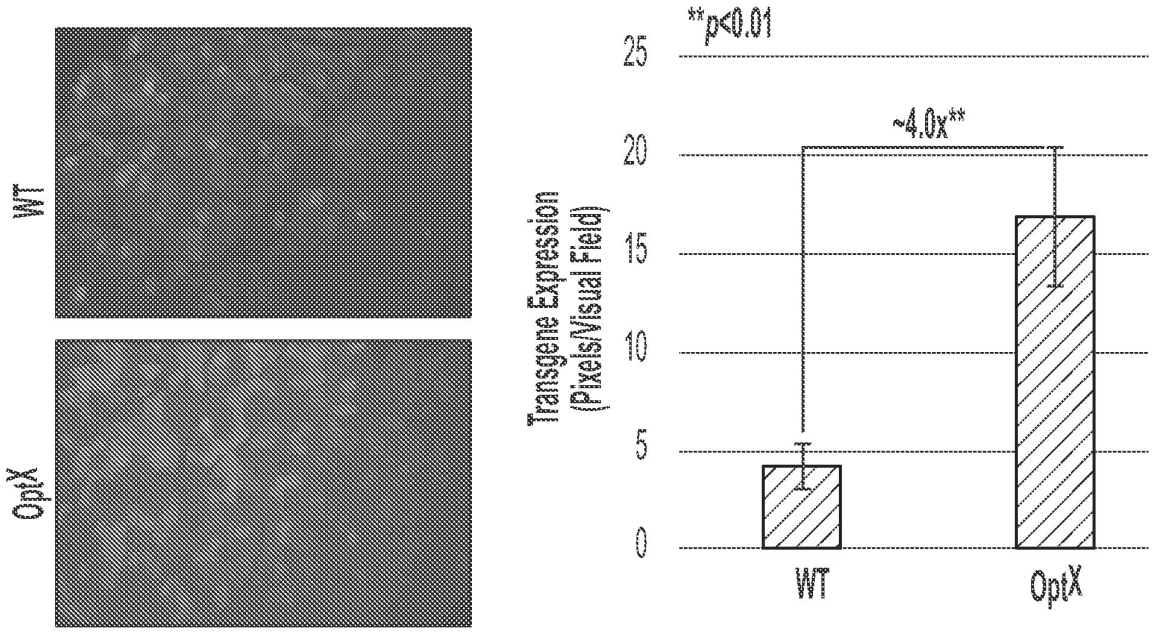

WT
OptX
**p<0.01
~4.0x**
Transgene Expression
(Pixels/Visual Field)
25
20
15
10
5
0
WT
OptX

FIG. 7A

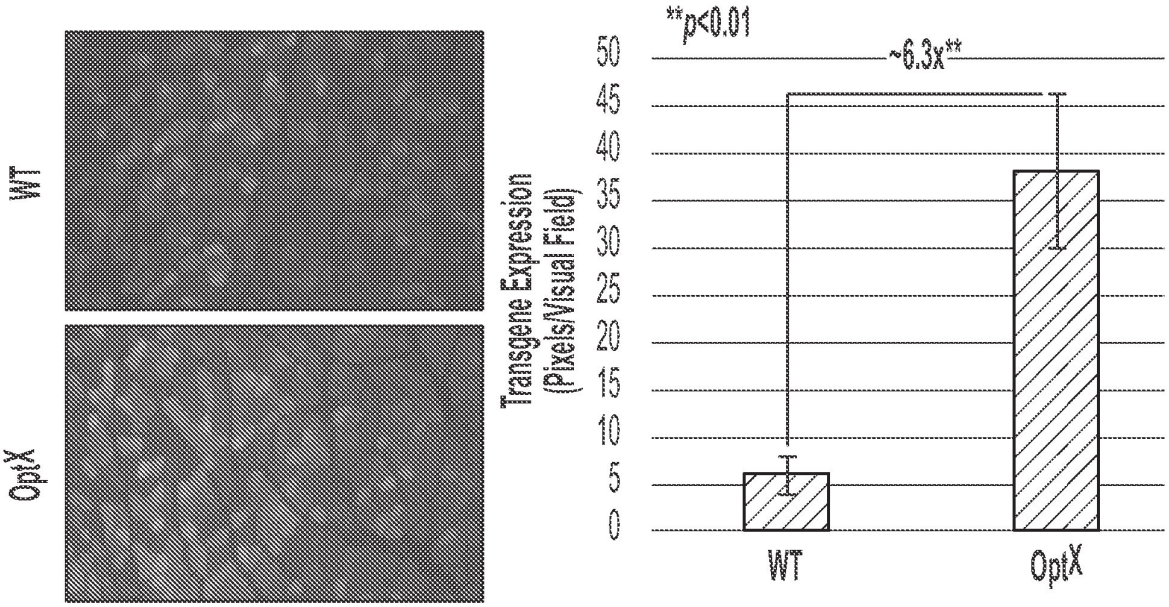

WT
OptX
**p<0.01
~6.3x**
Transgene Expression
(Pixels/Visual Field)
50
45
40
35
30
25
20
15
10
5
0
WT
OptX

FIG. 7B

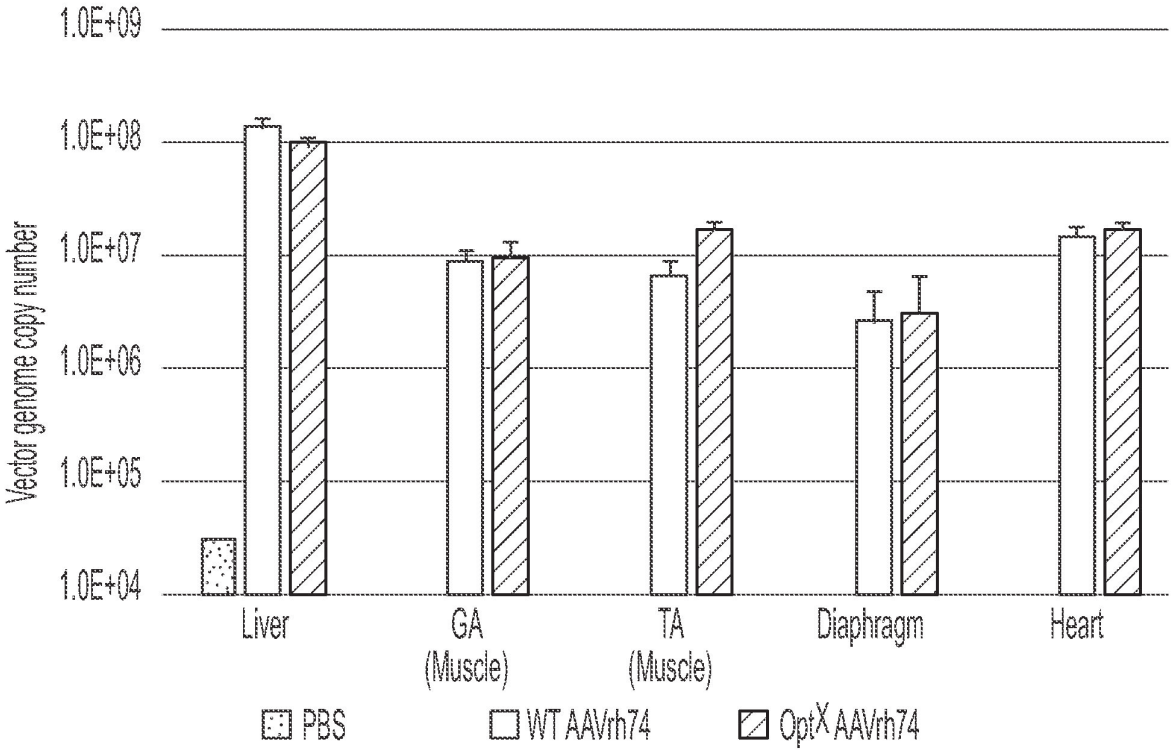

1.0E+09
1.0E+08
1.0E+07
1.0E+06
1.0E+05
1.0E+04
Vector genome copy number
Liver
GA (Muscle)
TA (Muscle)
Diaphragm
Heart
PBS
WT AAVrh74
Opt^X AAVrh74

FIG. 7C

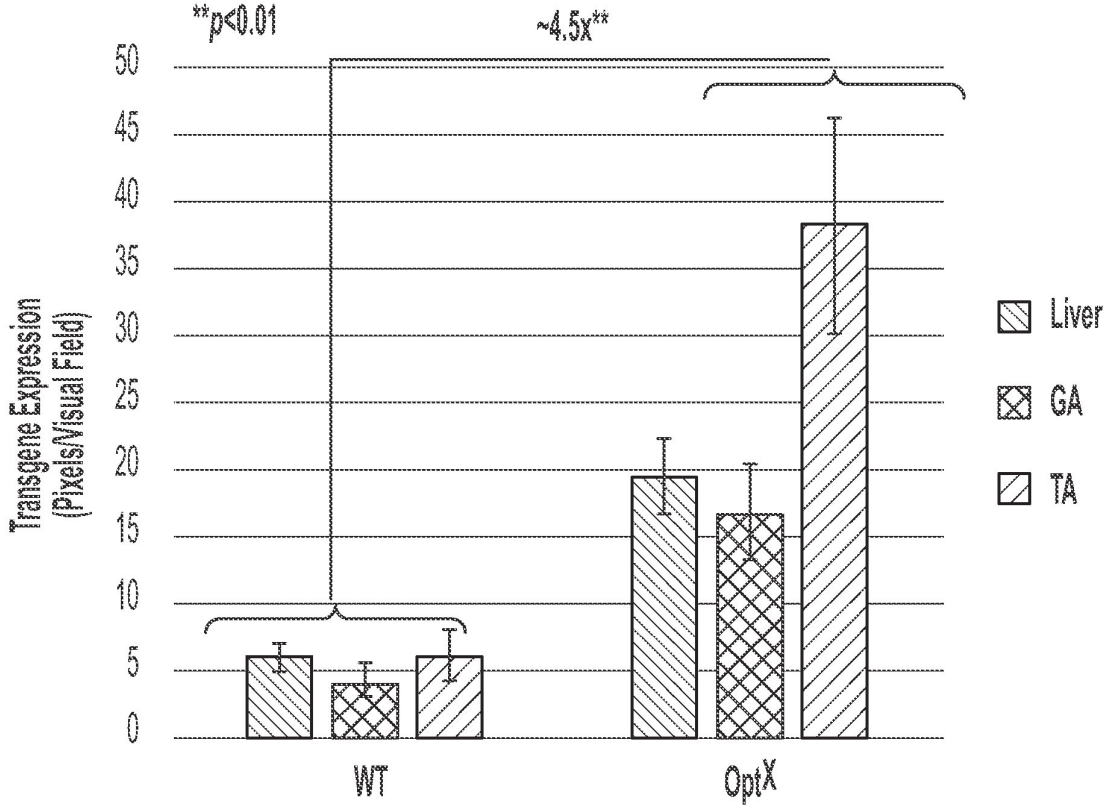

**p<0.01
~4.5x**
50
45
40
35
30
25
20
15
10
5
0
Transgene Expression (Pixels/Visual Field)
WT
Opt^X
Liver
GA
TA

FIG. 7D

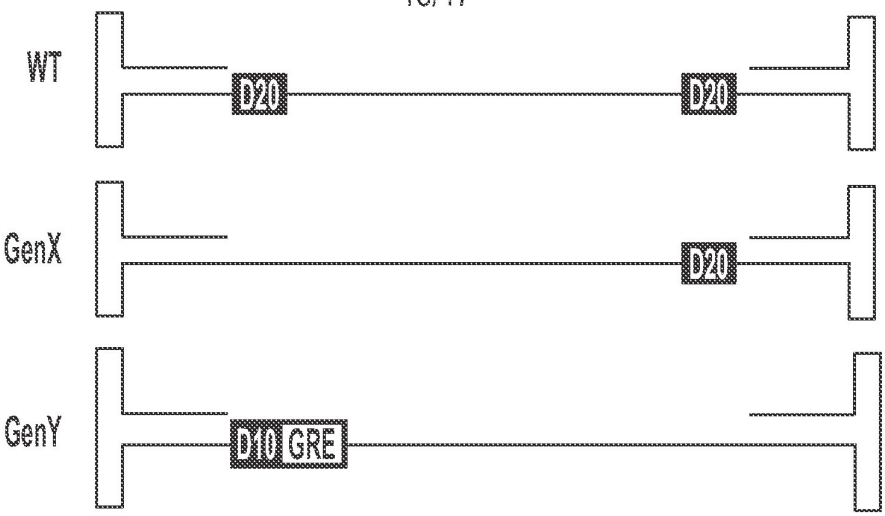
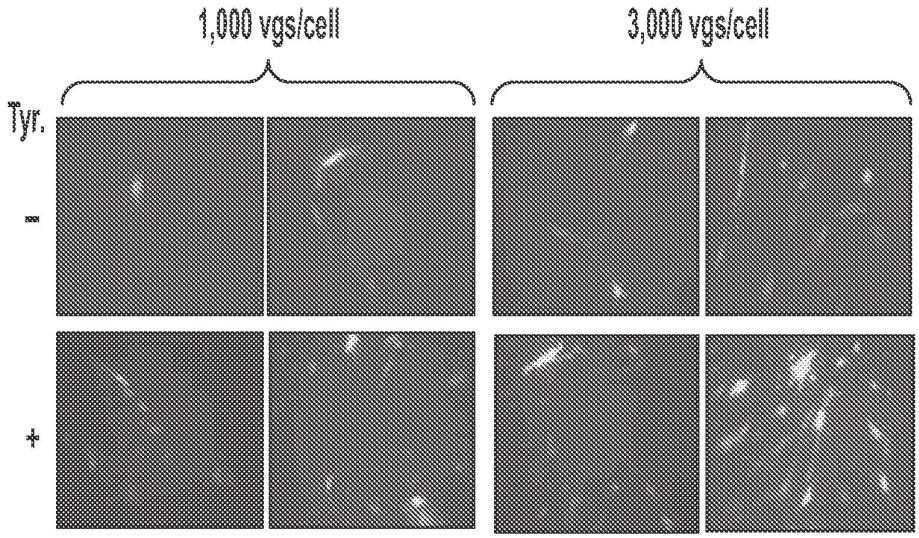

WT
D20
D20
GenX
D20
GenY
D10
GRE

FIG. 8A


1,000 vgs/cell
3,000 vgs/cell
Tyr.
-
+

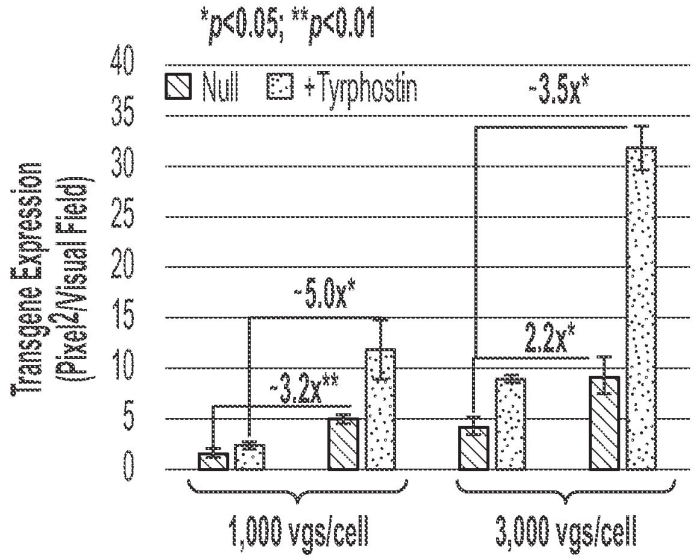

*p<0.05; **p<0.01
Null
+Tyrphostin
~3.5x*
~5.0x*
2.2x*
~3.2x**
Transgene Expression
(Pixel^2/Visual Field)
40
35
30
25
20
15
10
5
0
1,000 vgs/cell
3,000 vgs/cell

FIG. 8B

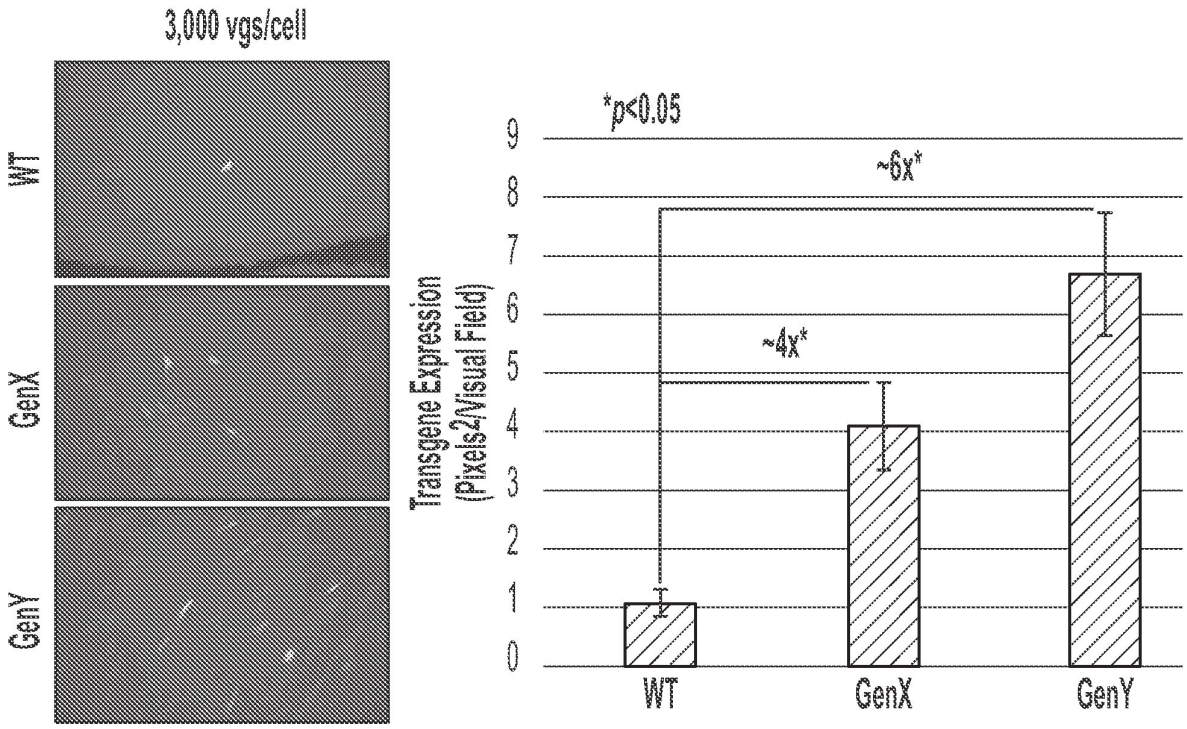

3,000 vgs/cell
WT
GenX
GenY
*p<0.05
~6x*
~4x*
Transgene Expression
(Pixels2/Visual Field)
0
1
2
3
4
5
6
7
8
9
WT
GenX
GenY

FIG. 8C

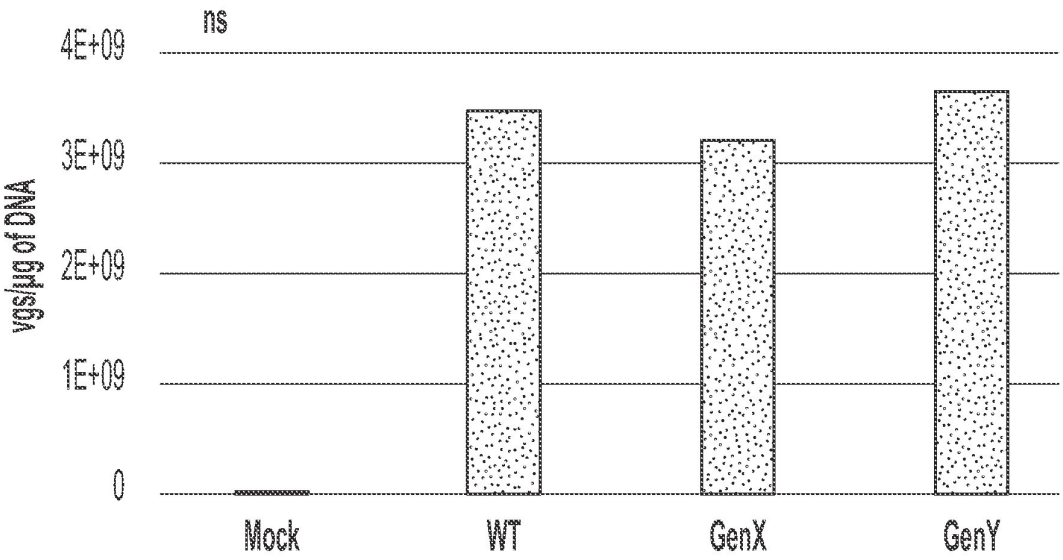

ns
4E+09
3E+09
2E+09
1E+09
0
vgs/µg of DNA
Mock
WT
GenX
GenY

FIG. 8D

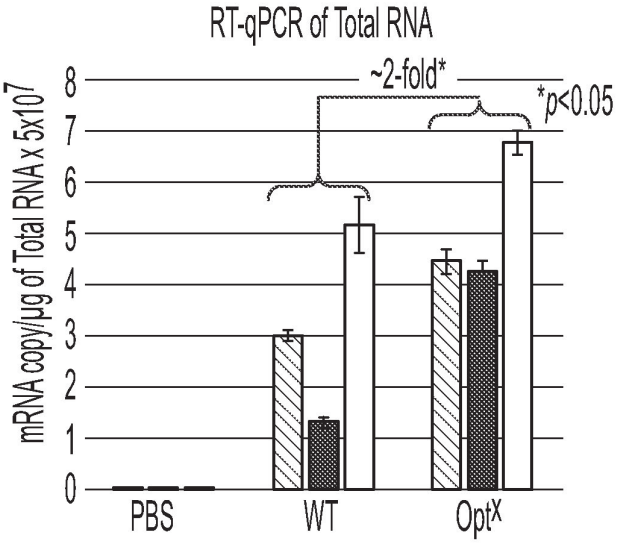


FIG. 9A

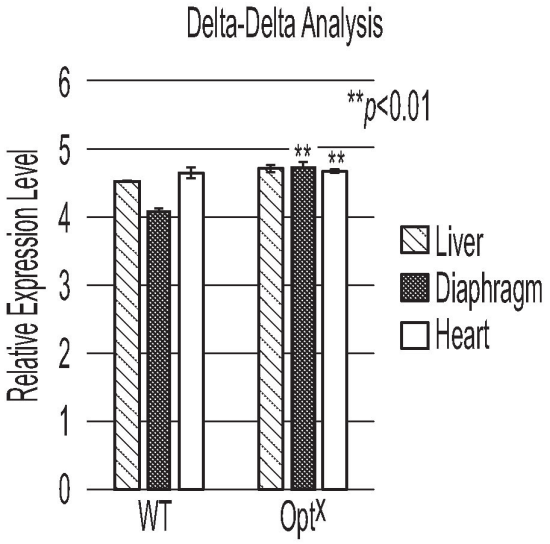


FIG. 9B

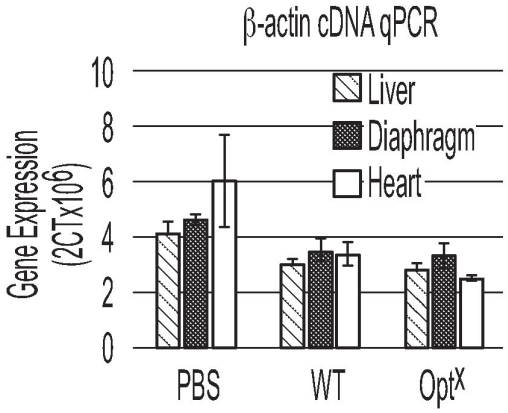


FIG. 10A

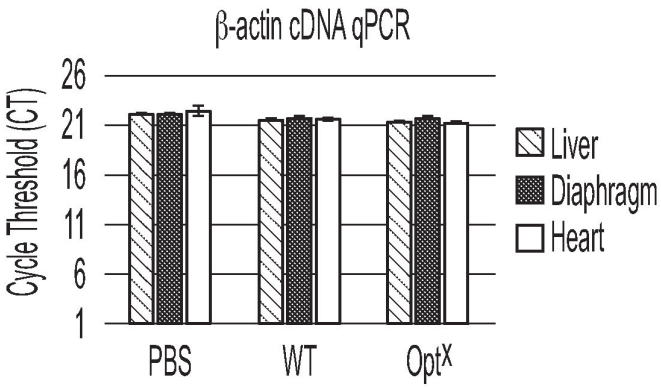


FIG. 10B

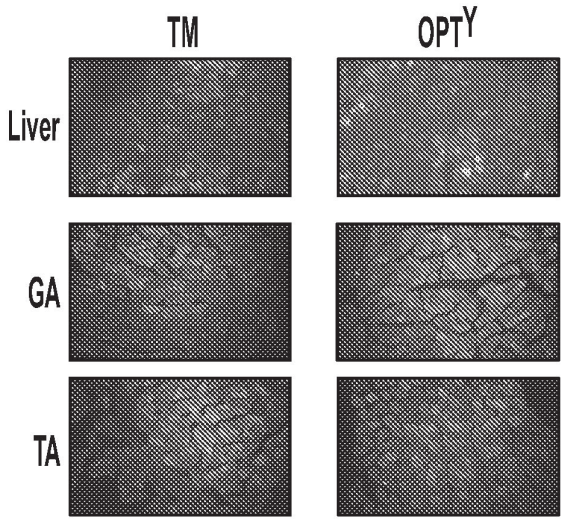


FIG. 11A

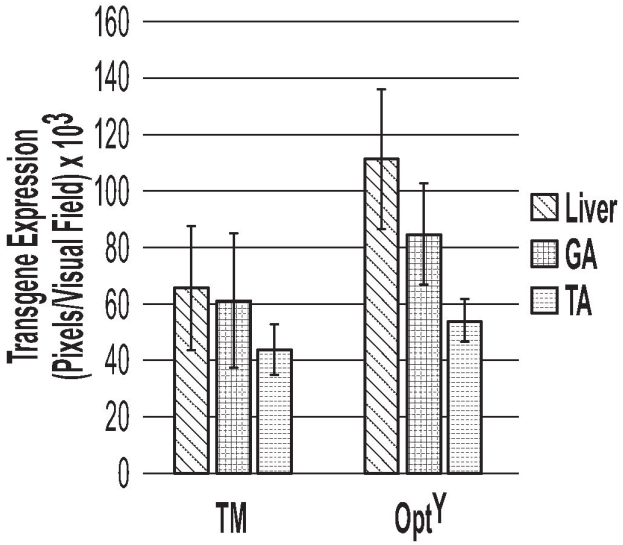


FIG. 11B

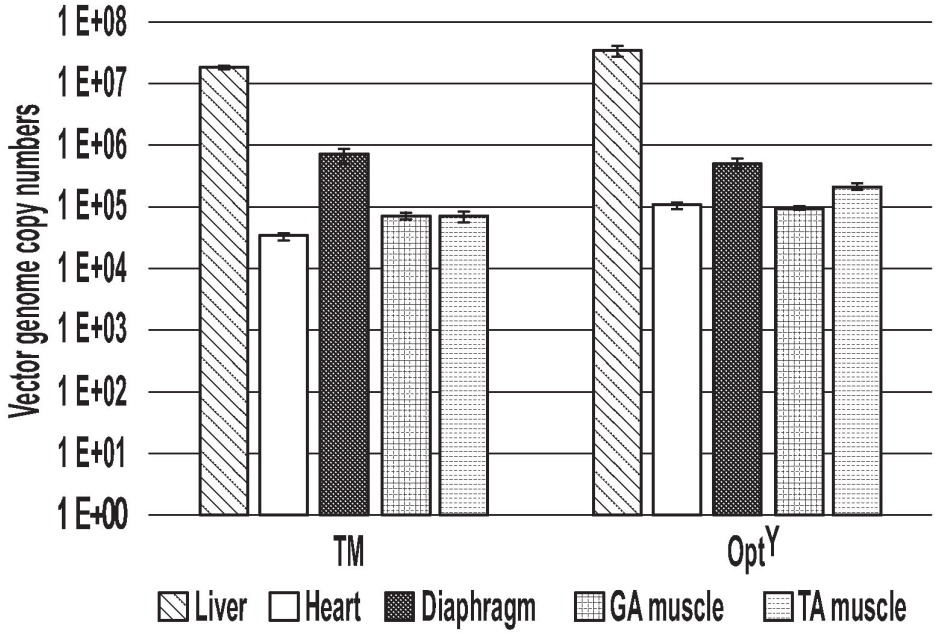


FIG. 12

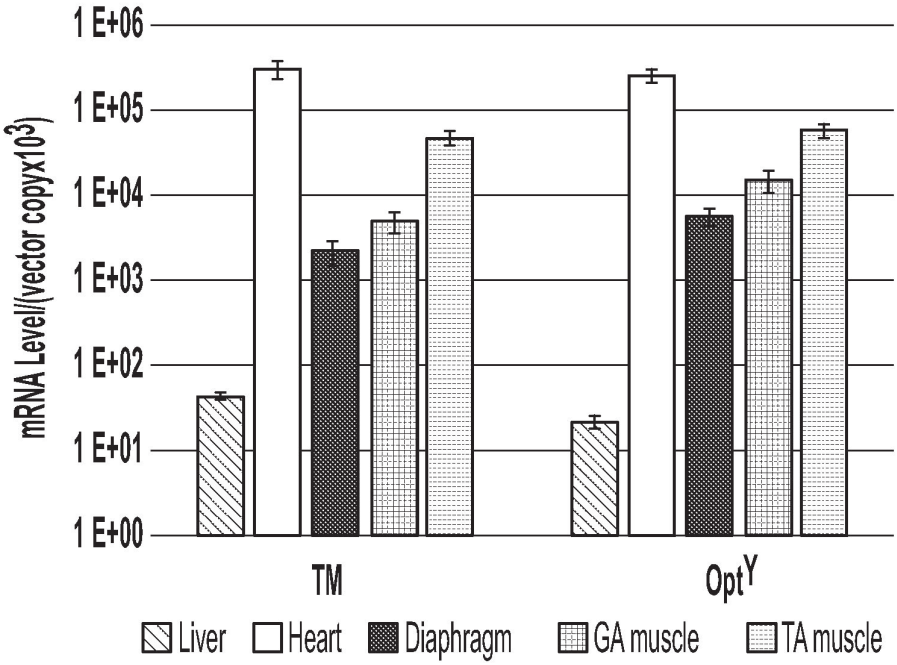

1 E+06
1 E+05
1 E+04
1 E+03
1 E+02
1 E+01
1 E+00
mRNA Level//(vector copyx10^3)
TM
Opt^Y
Liver
Heart
Diaphragm
GA muscle
TA muscle

FIG. 13