FIG. 1A

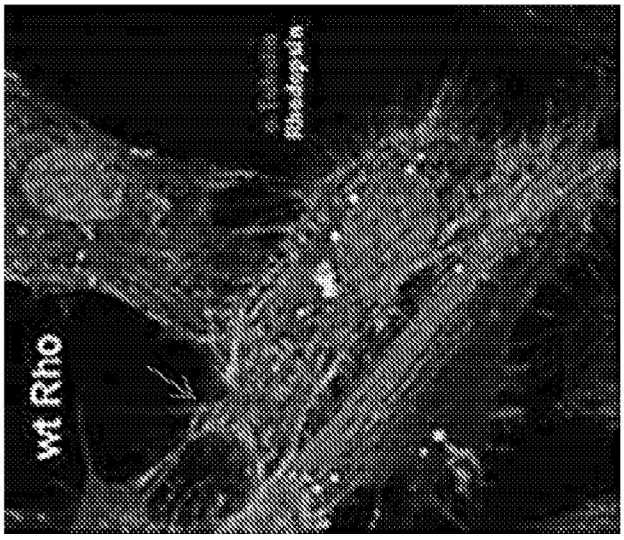
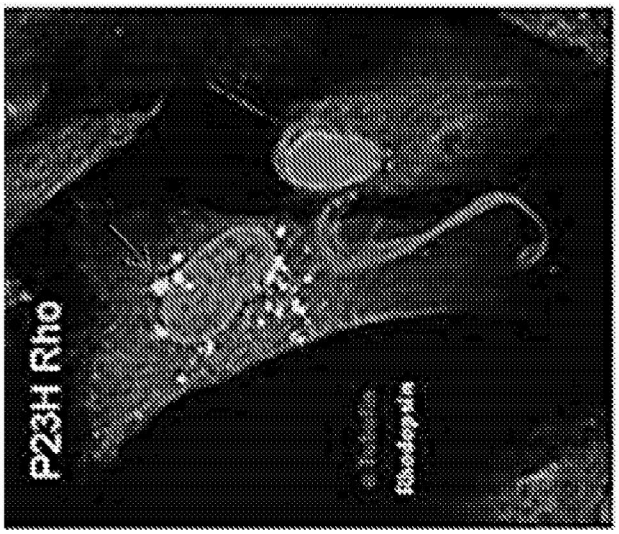


FIG. 1B



FIGS. 1A & 1B

FIG. 2A

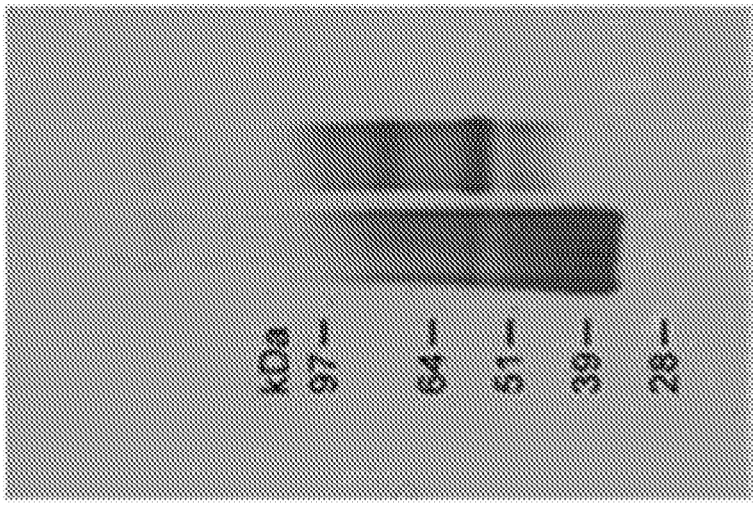
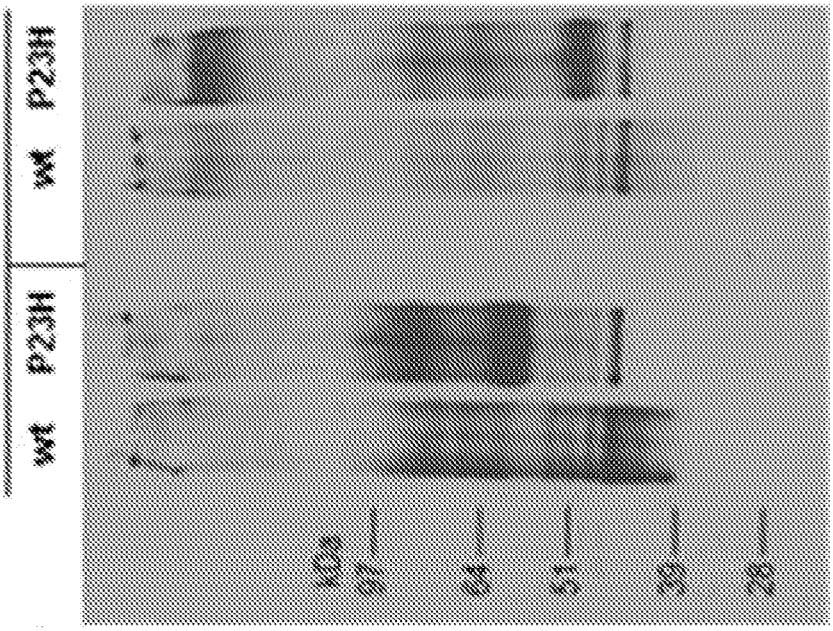


FIG. 2B



FIGS. 2A & 2B

FIG. 3A

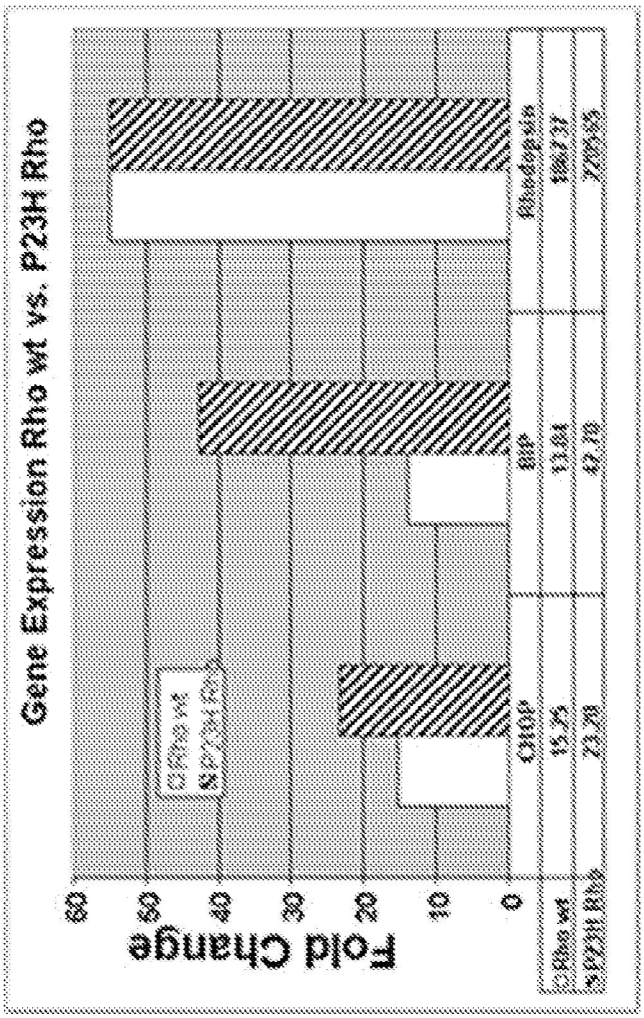
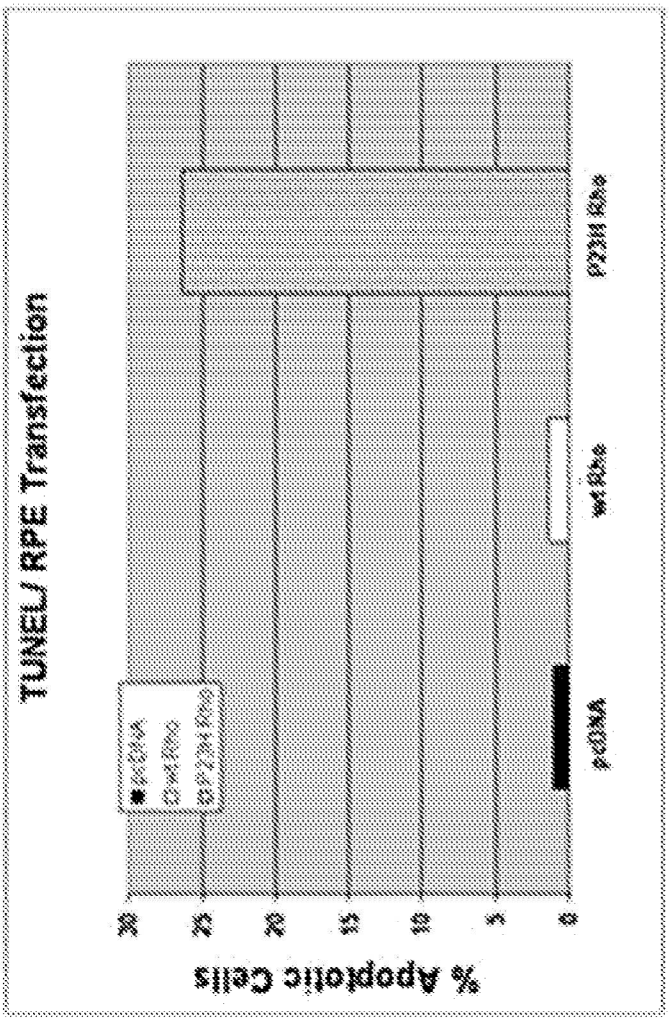


FIG.3B



FIGS. 3A & 3B

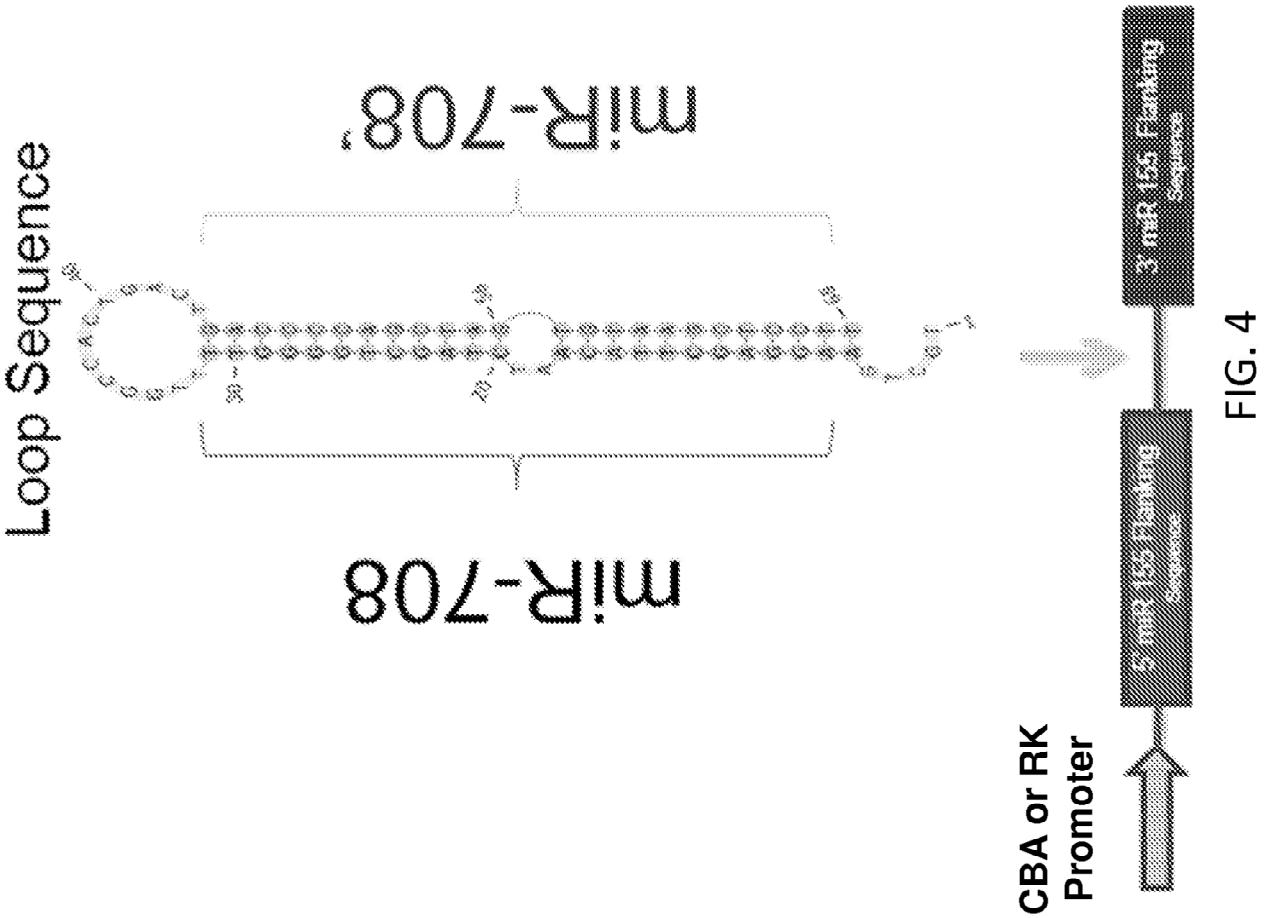

Loop Sequence
miR-708
miR-708'
CBA or RK Promoter
5' miR 155 Flanking Sequence
3 miR 155 Flanking Sequence

FIG. 4

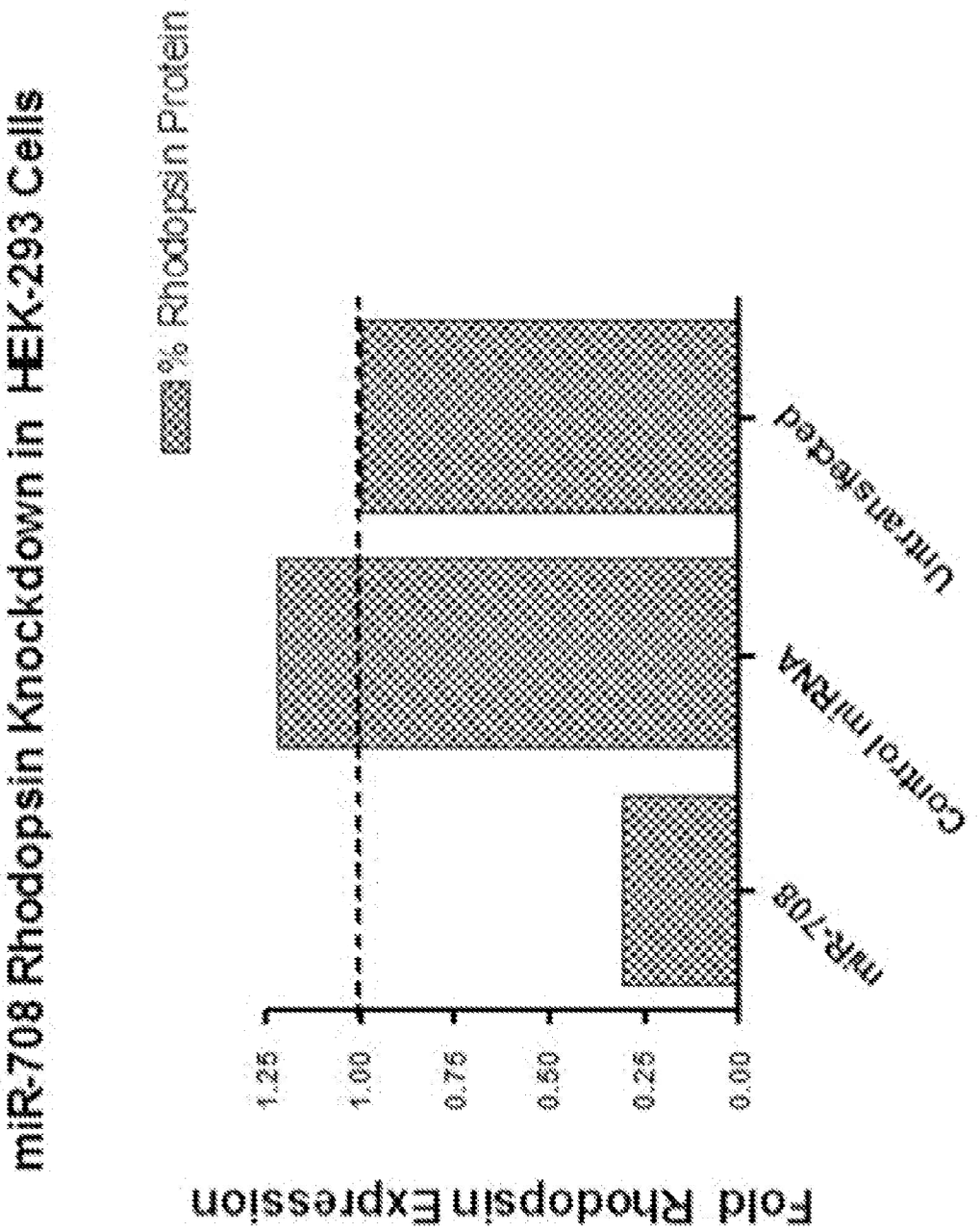

miR-708 Rhodopsin Knockdown in HEK-293 Cells
% Rhodopsin Protein
Fold Rhodopsin Expression
1.25
1.00
0.75
0.50
0.25
0.00
miR-708
Control miRNA
Untransfected

FIG. 5

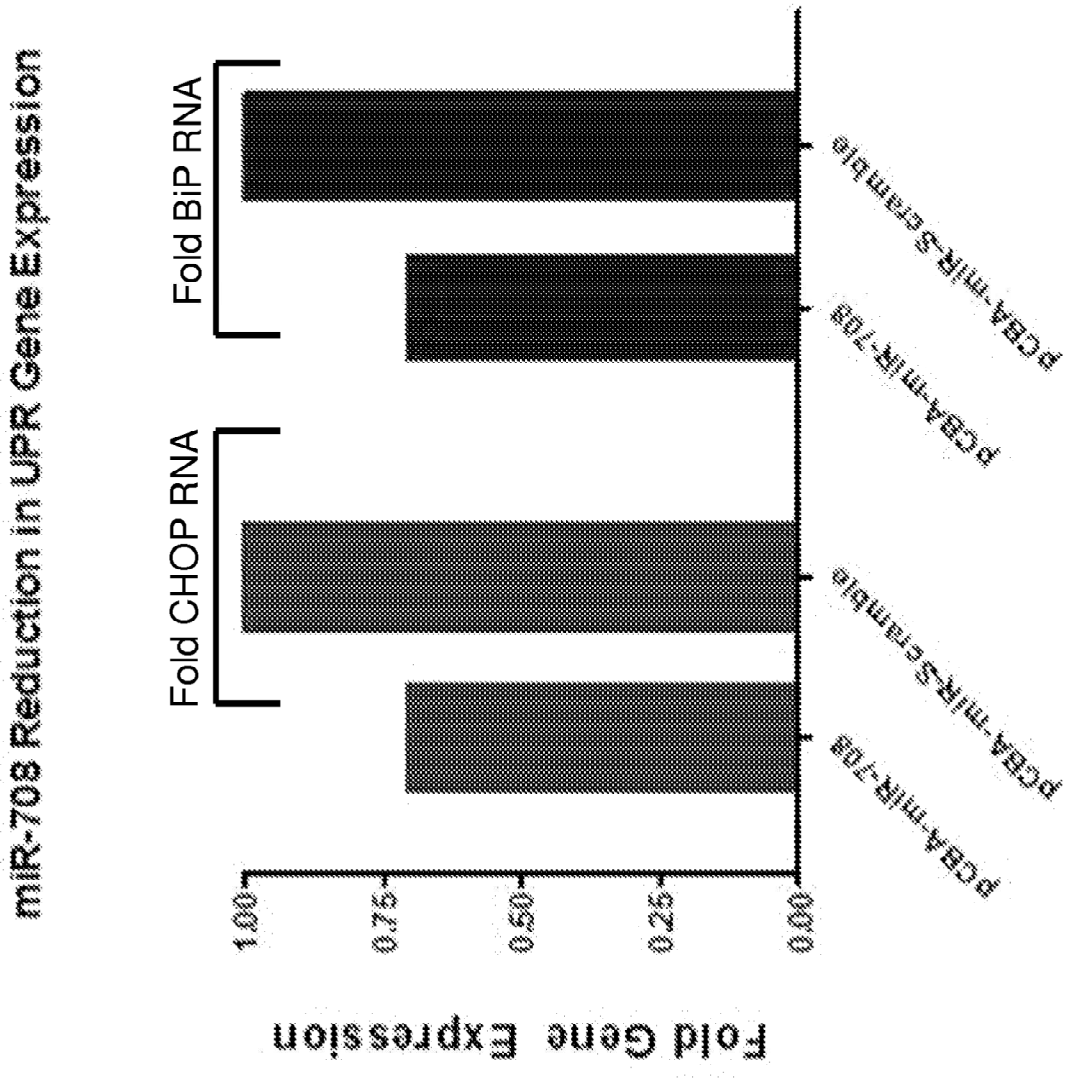

miR-708 Reduction in UPR Gene Expression
Fold Gene Expression
1.00
0.75
0.50
0.25
0.00
Fold CHOP RNA
Fold BiP RNA
pCBA-miR-708
pCBA-miR-Scramble
pCBA-miR-708
pCBA-miR-Scramble

FIG. 6

FIG. 7A

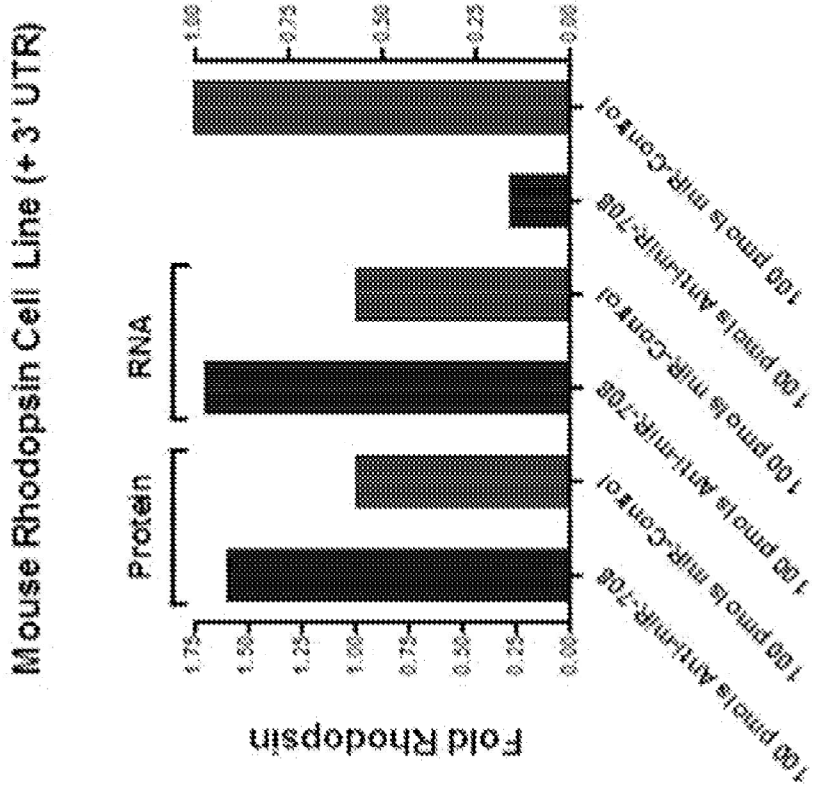
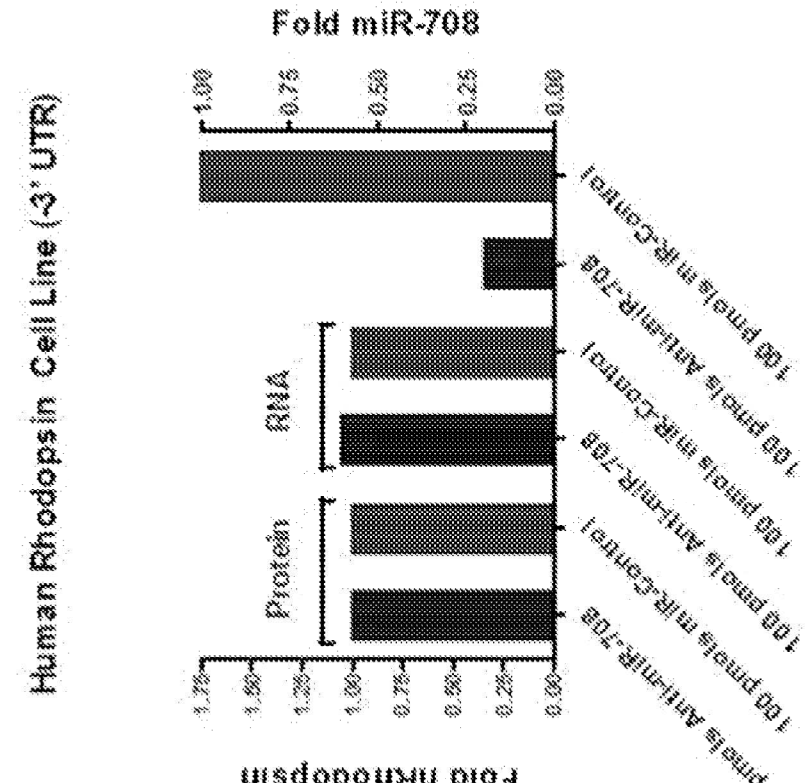


FIG. 7B



FIGS. 7A & 7B

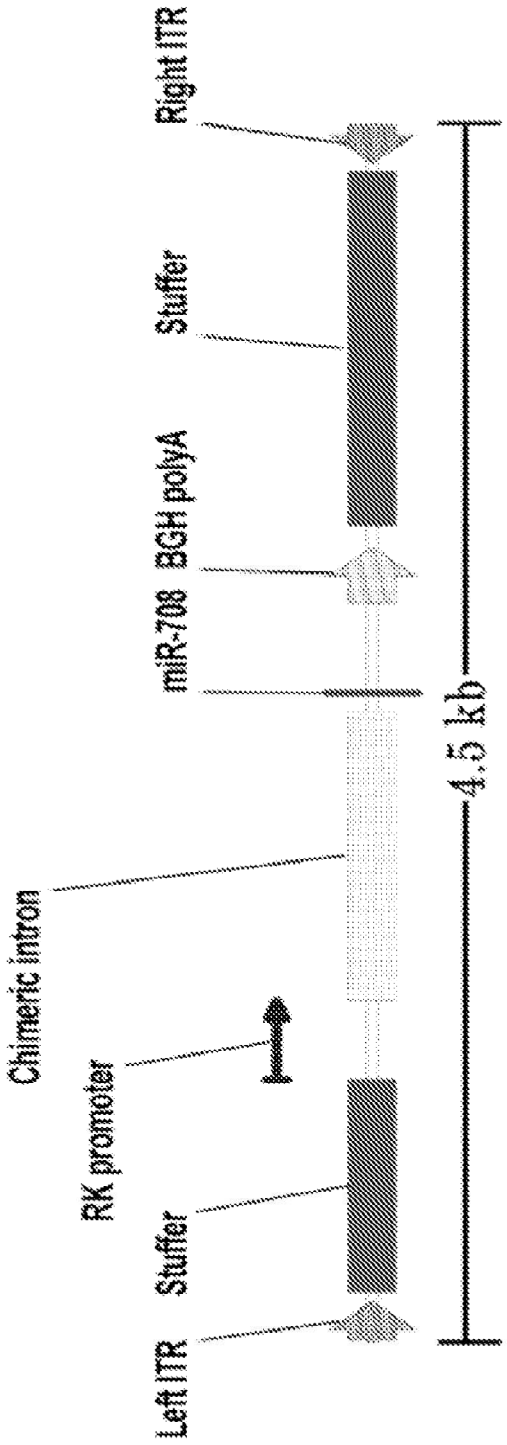

Left ITR
Stuffer
RK promoter
Chimeric intron
miR-708
BGH polyA
Stuffer
Right ITR
4.5 kb

FIG. 8

FIG. 9A

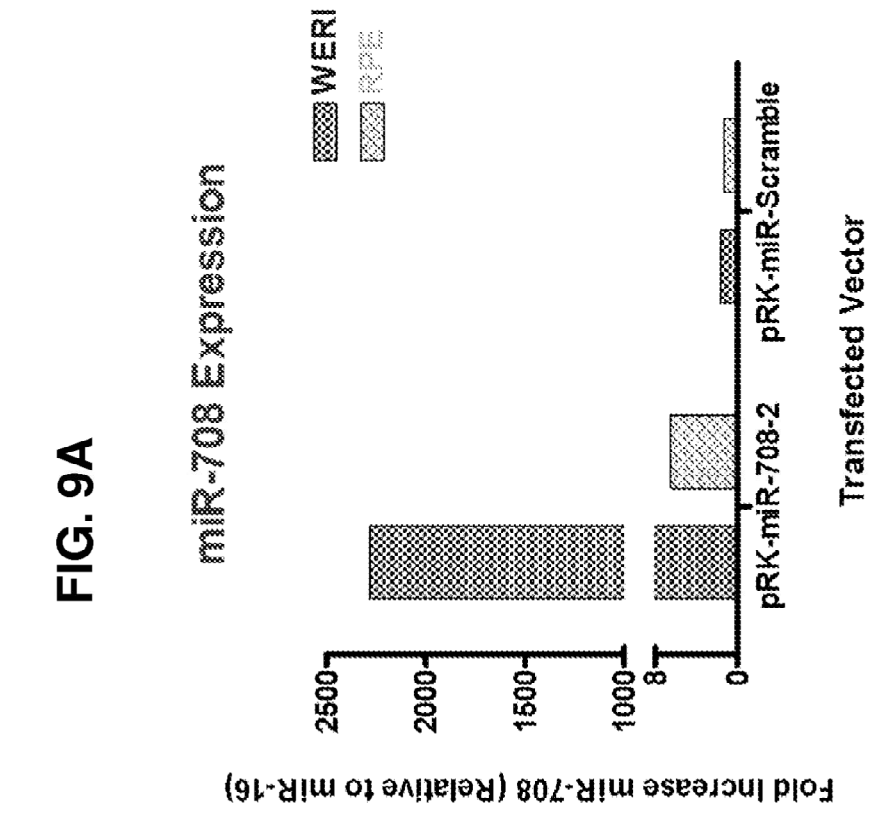
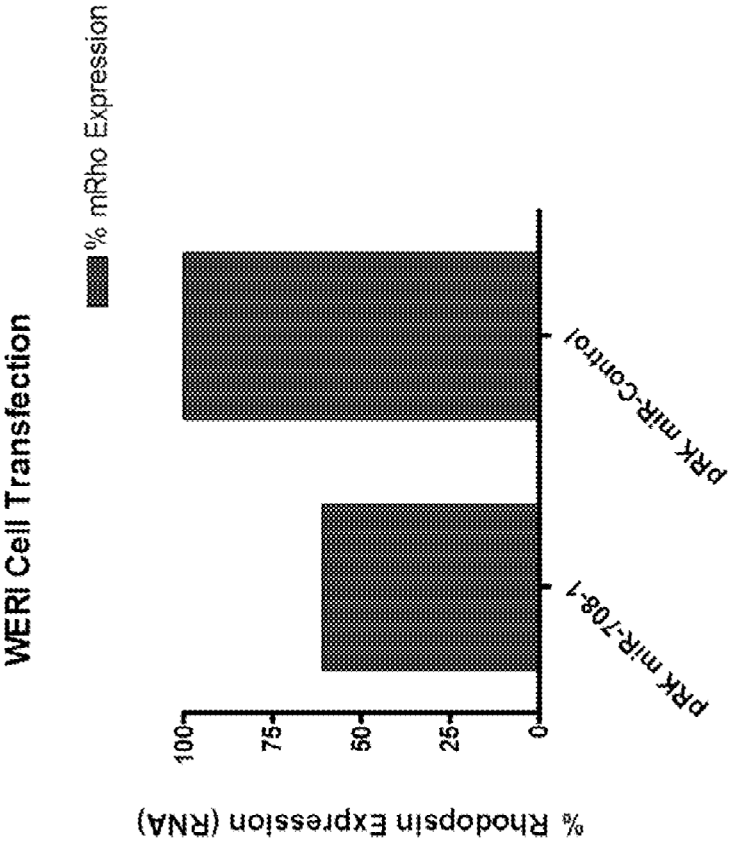
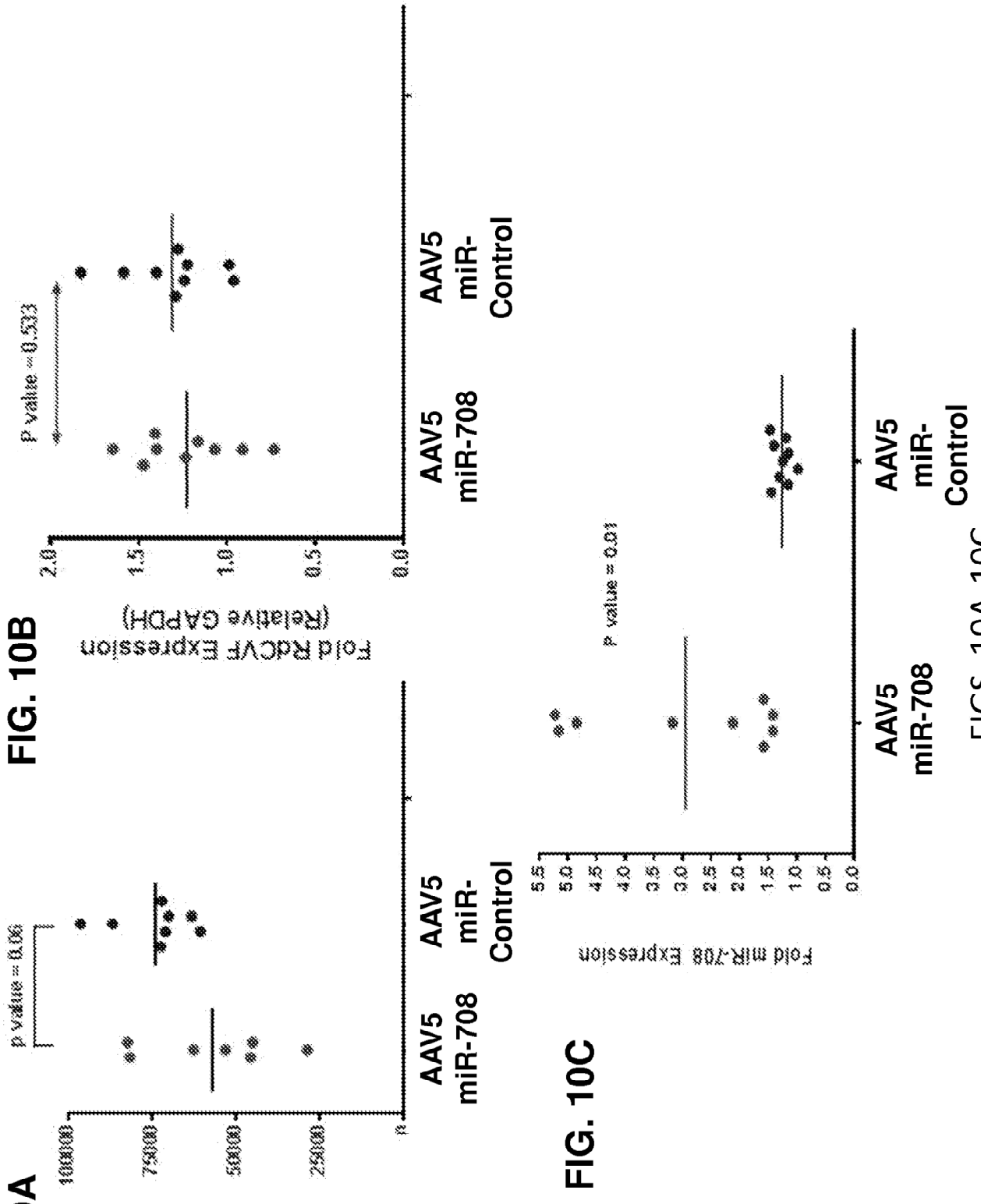


FIG. 9B



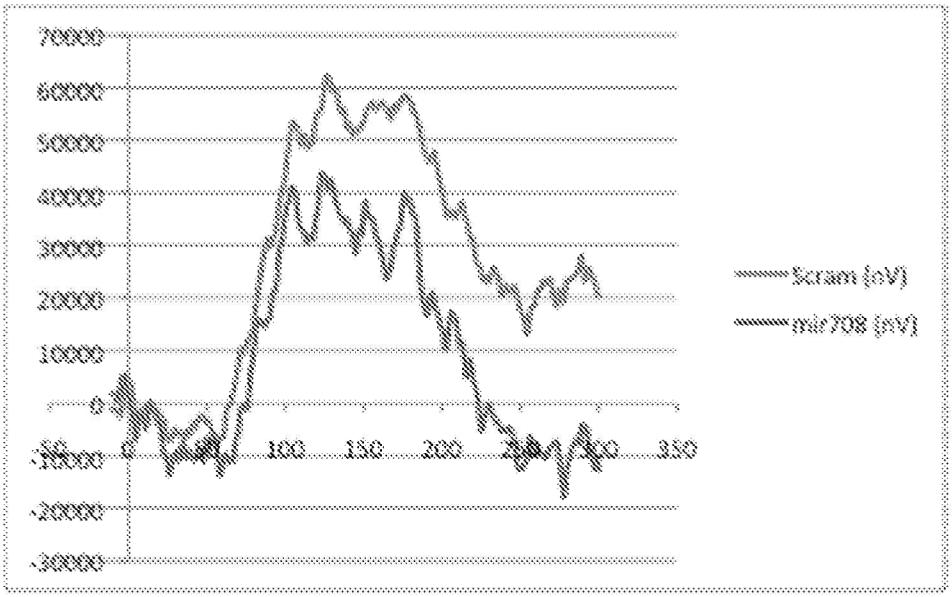
FIGS. 9A & 9B


FIG.10A
p value = 0.06
Copies mRho/ µg
100000
75000
50000
25000
0
AAV5 miR-708
AAV5 miR-Control
FIG. 10B
P value = 0.533
Fold RdCVF Expression (Relative GAPDH)
2.0
1.5
1.0
0.5
0.0
AAV5 miR-708
AAV5 miR-Control
FIG. 10C
P value = 0.01
Fold miR-708 Expression
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
AAV5 miR-708
AAV5 miR-Control

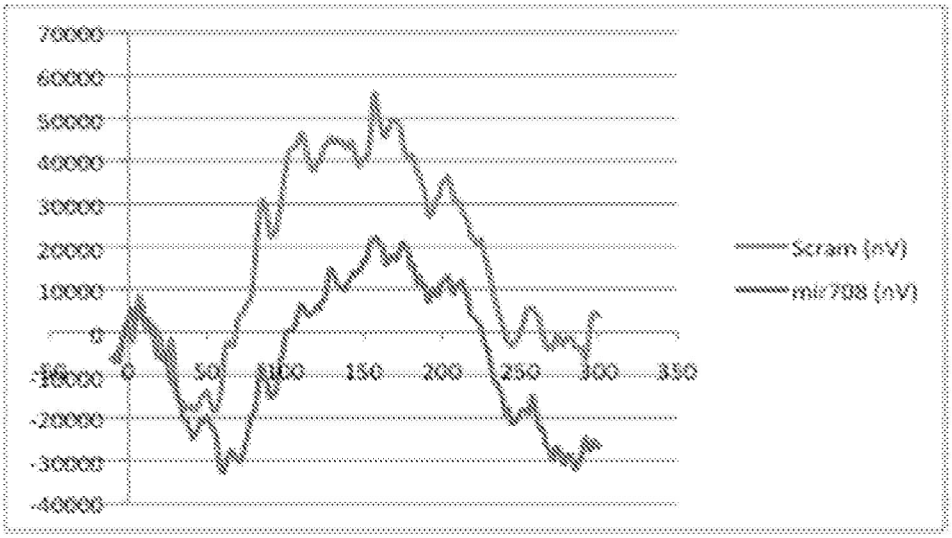
FIGS. 10A-10C

FIG. 11A

Animal # 45595



Animal # 45596



Animal # 45599

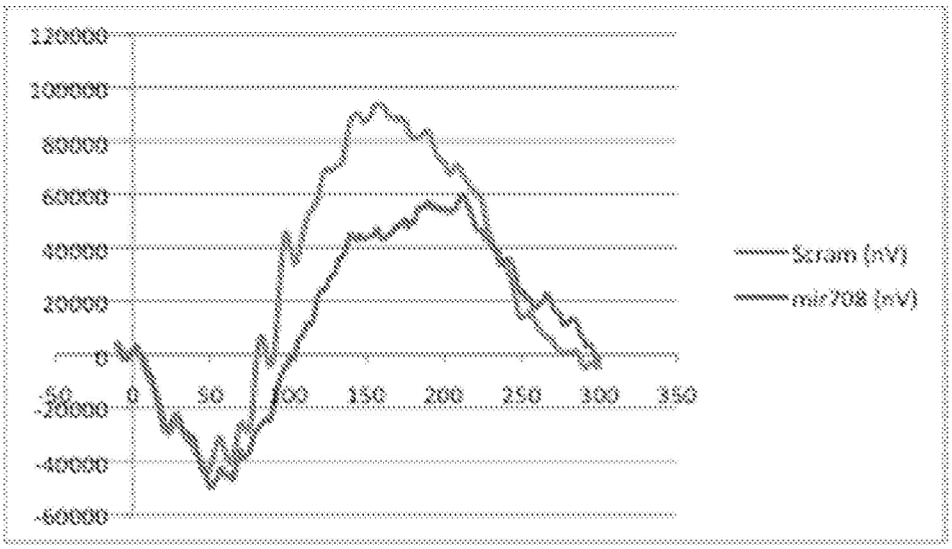
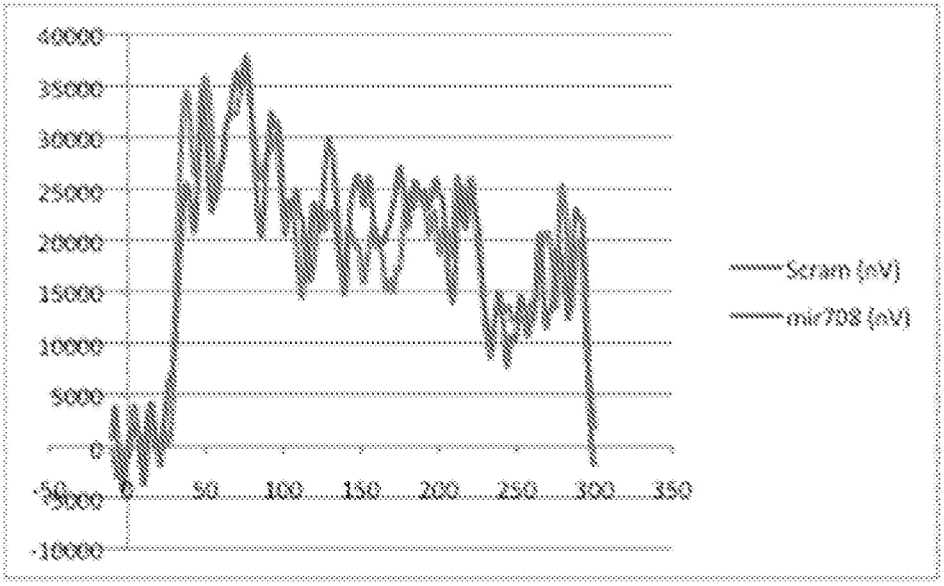
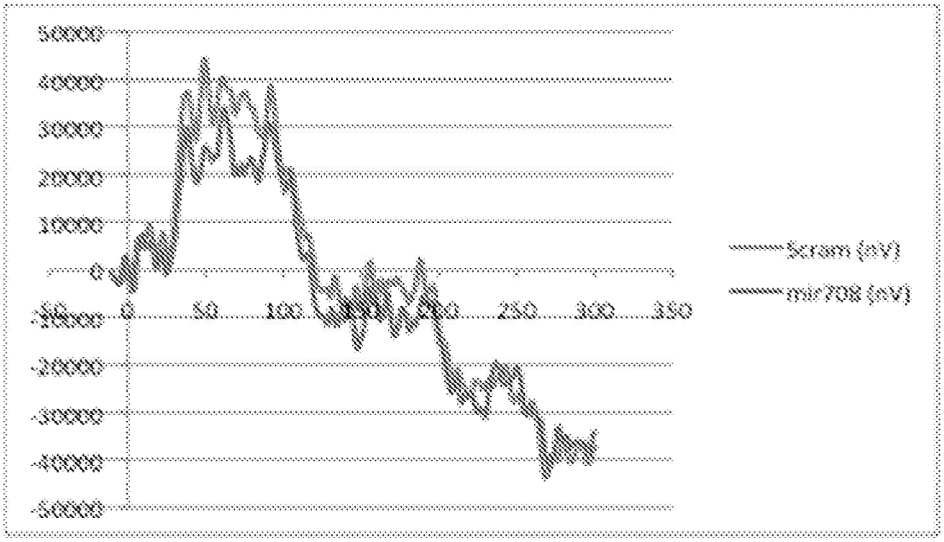


FIG. 11B

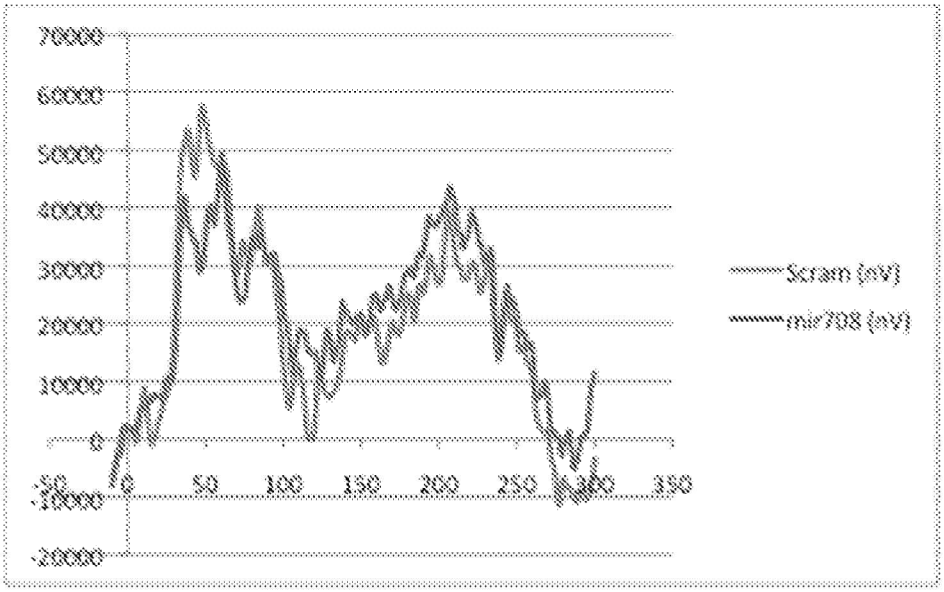
Animal # 45595



Animal # 45596



Animal # 45599



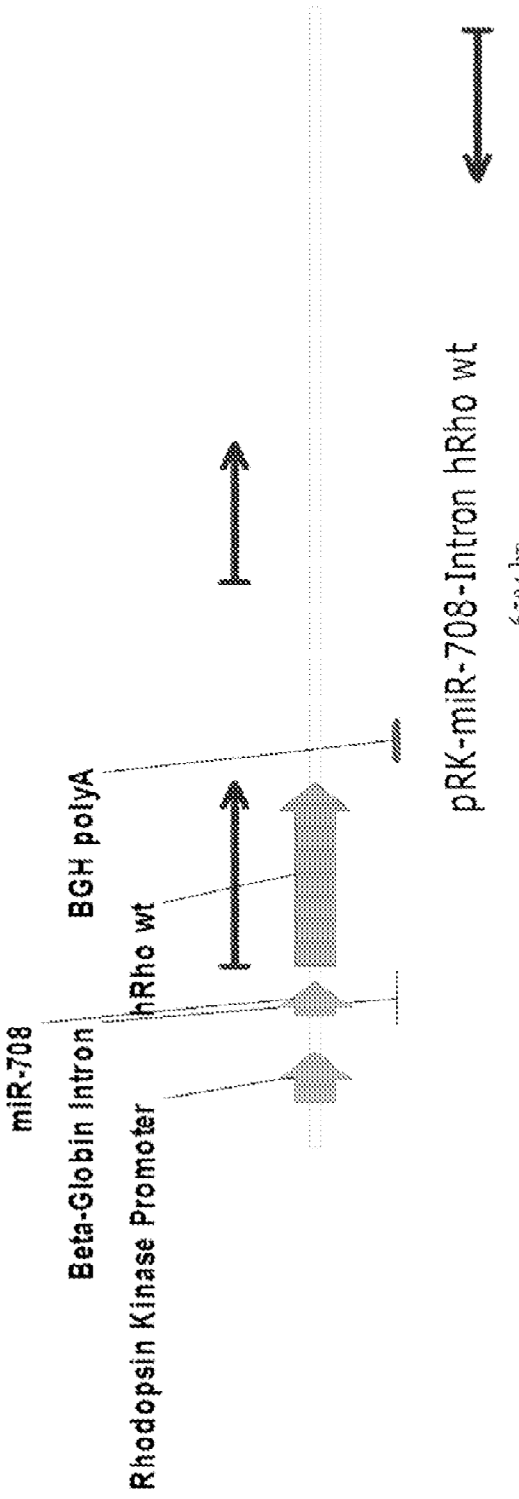

miR-708
Beta-Globin Intron
Rhodopsin Kinase Promoter
hRho wt
BGH polyA
pRK-miR-708-Intron hRho wt
6524 bp

FIG. 12

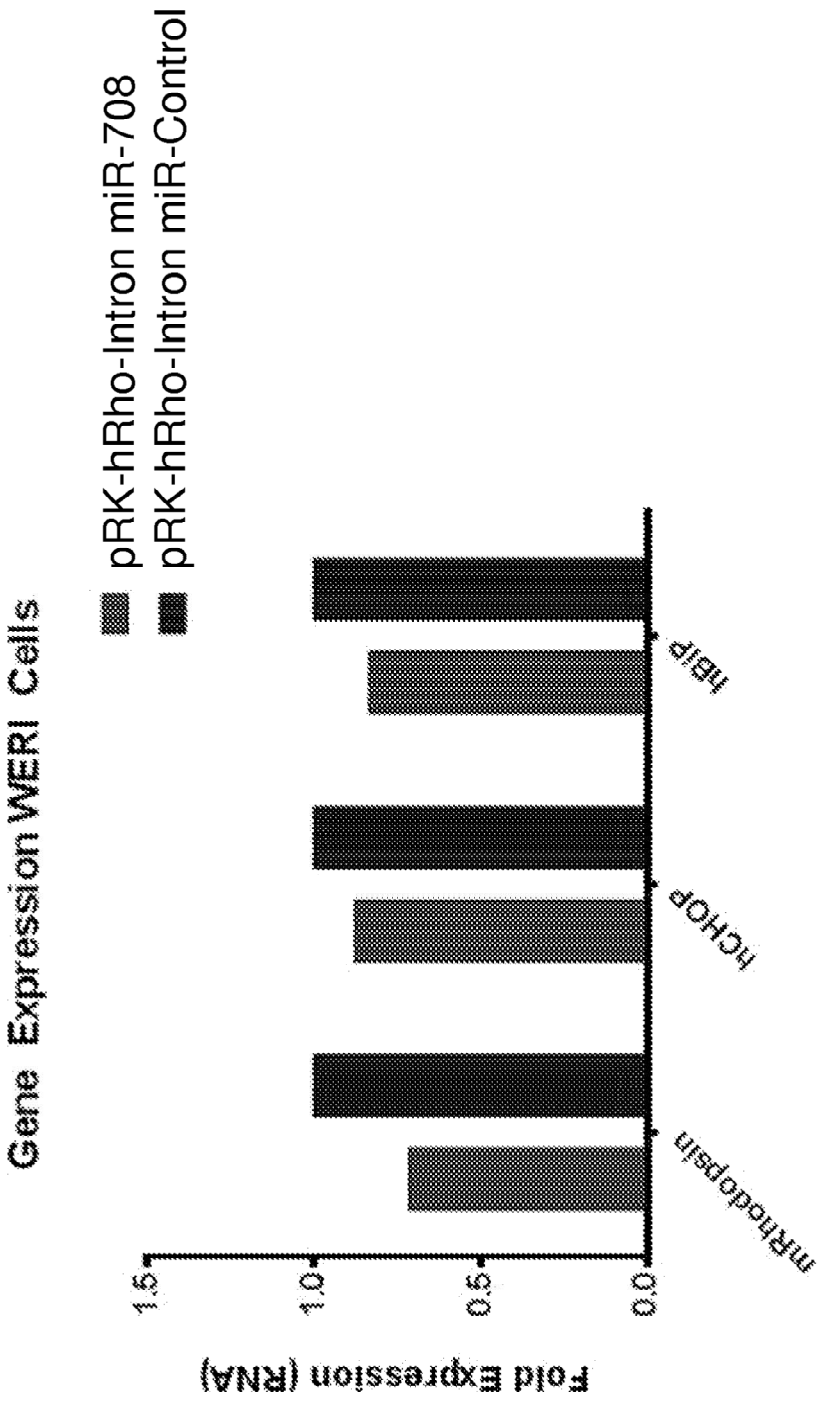

Gene Expression WERI Cells
pRK-hRho-Intron miR-708
pRK-hRho-Intron miR-Control
Fold Expression (RNA)
1.5
1.0
0.5
0.0
mRhodopsin
hCHOP
hBiP

FIG. 13

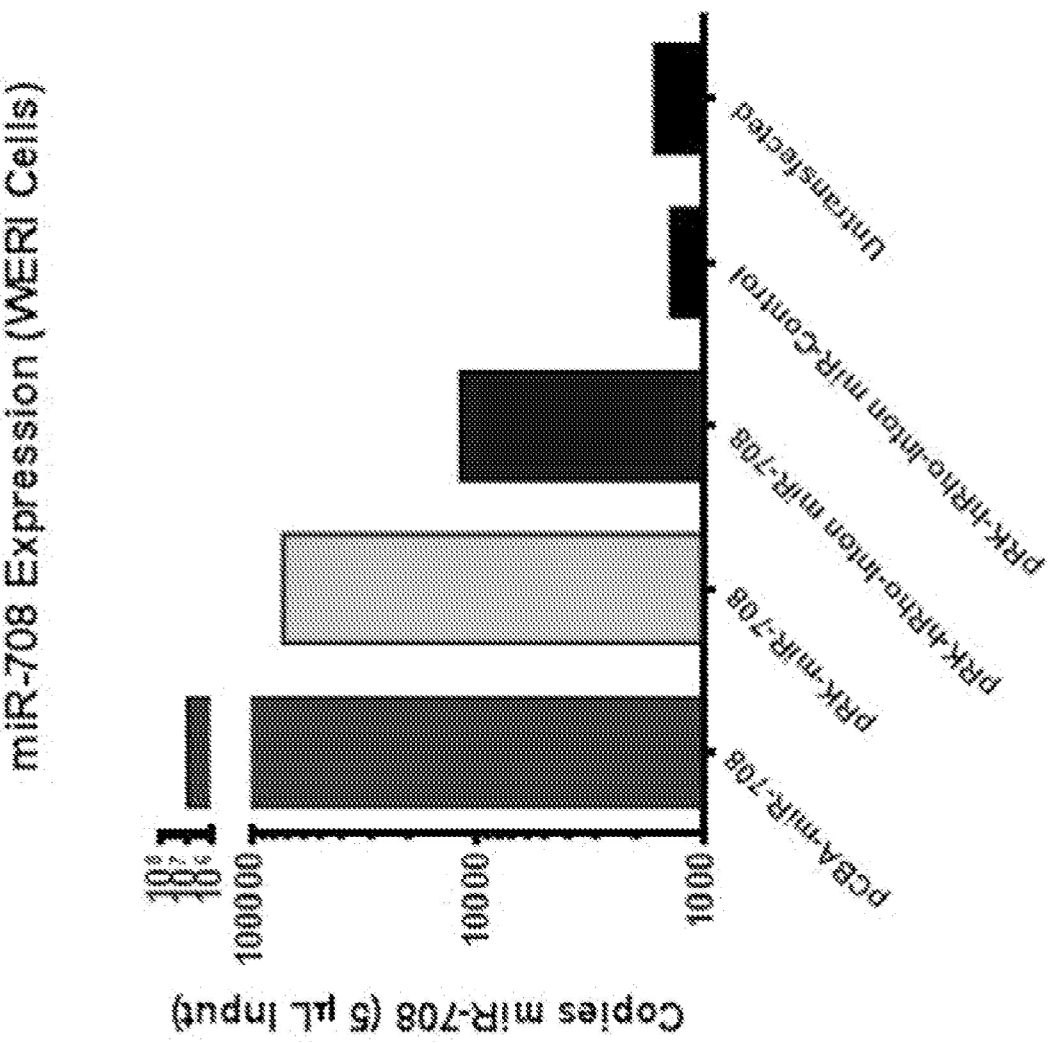

miR-708 Expression (WERI Cells)
Copies miR-708 (5 µL Input)
100000
10000
1000
1
pCBA-miR-708
pRK-miR-708
pRK-hRho-Intron miR-708
pRK-hRho-Intron miR-Control
untransfected

FIG. 14

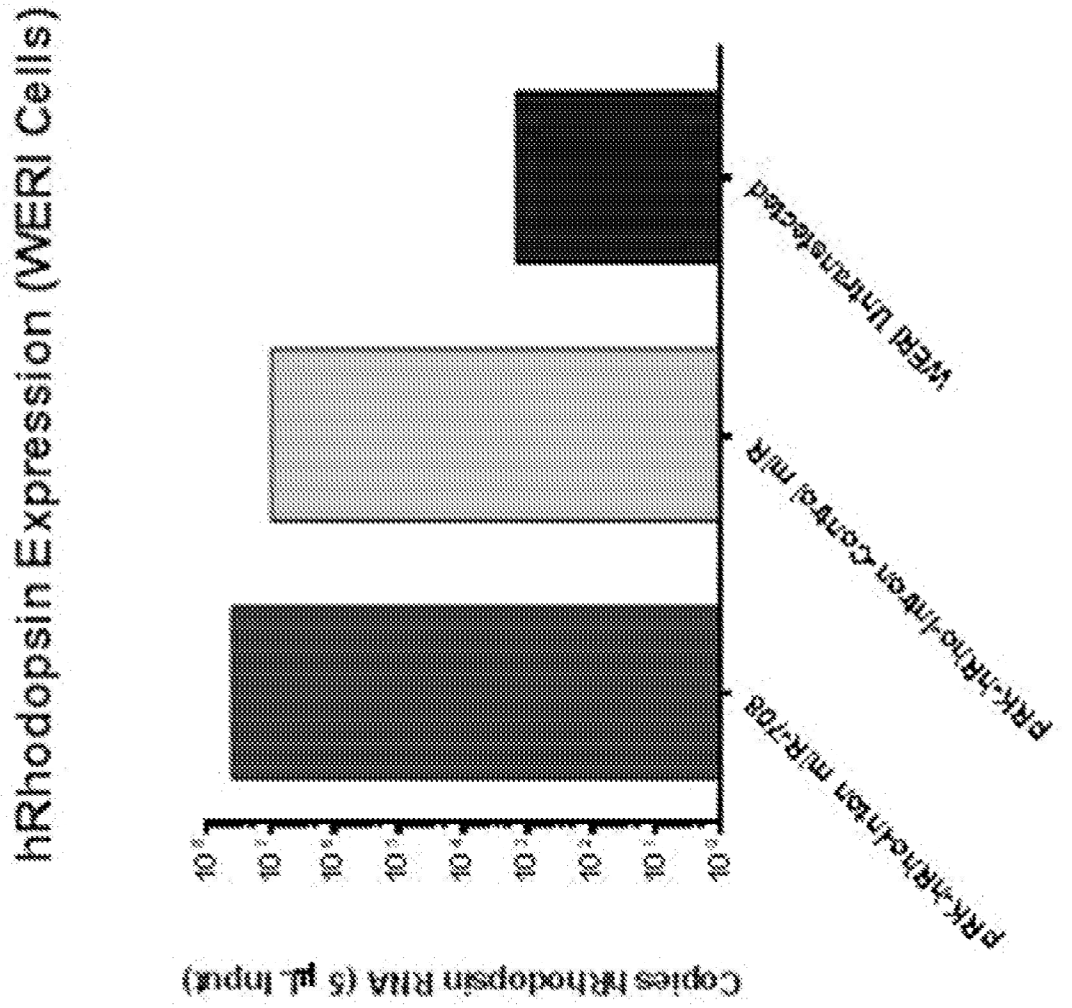

hRhodopsin Expression (WERI Cells)
Copies hRhodopsin RNA (5 µL Input)
0
10
10^2
10^3
10^4
10^5
10^6
10^7
10^8
PRK-hRho-hRho promoter miR-708
PRK-hRho-Hygro control miR
WERI Untransfected

FIG. 15

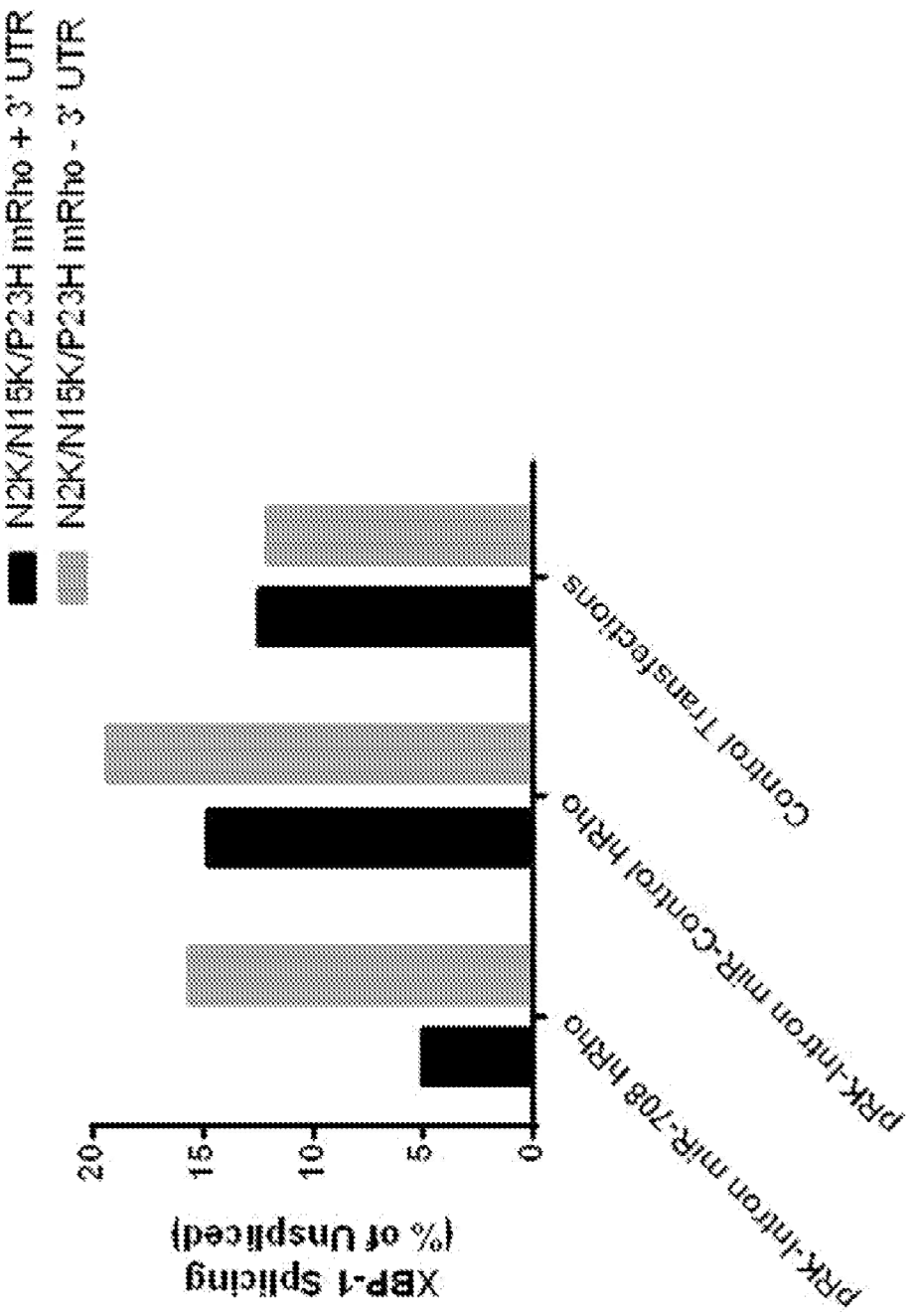

N2K/N15K/P23H mRho + 3' UTR
N2K/N15K/P23H mRho - 3' UTR
XBP-1 splicing
(% of Unspliced)
0
5
10
15
20
PRK-Intron miR-708 hRho
PRK-Intron miR-Control hRho
Control Transfections

FIG. 16

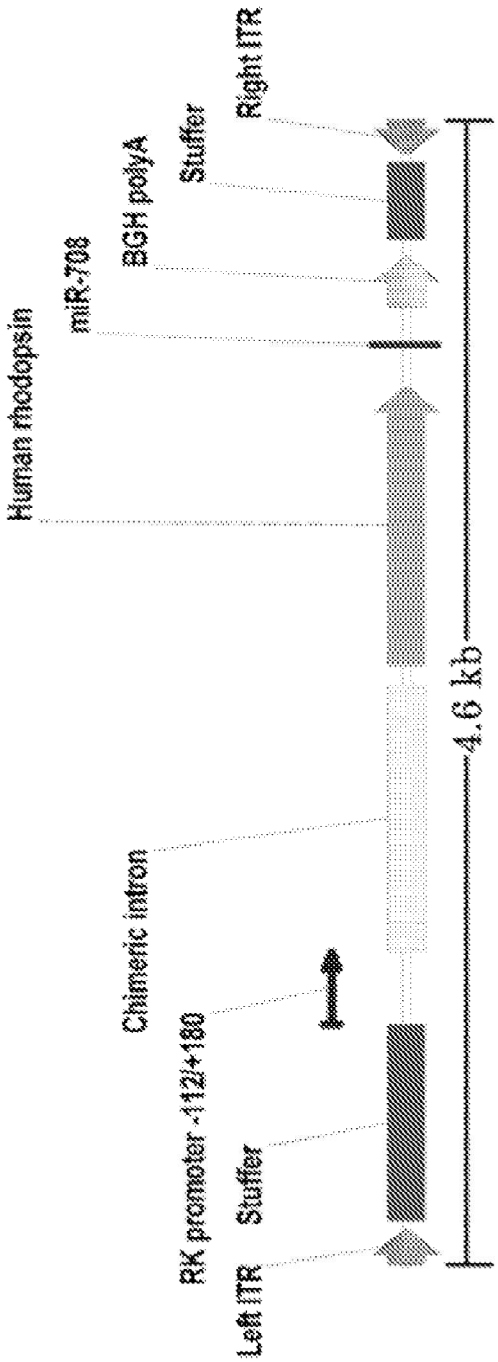

Left ITR
Stuffer
RK promoter -112/+180
Chimeric intron
Human rhodopsin
miR-708
BGH polyA
Stuffer
Right ITR
4.6 kb

FIG. 17

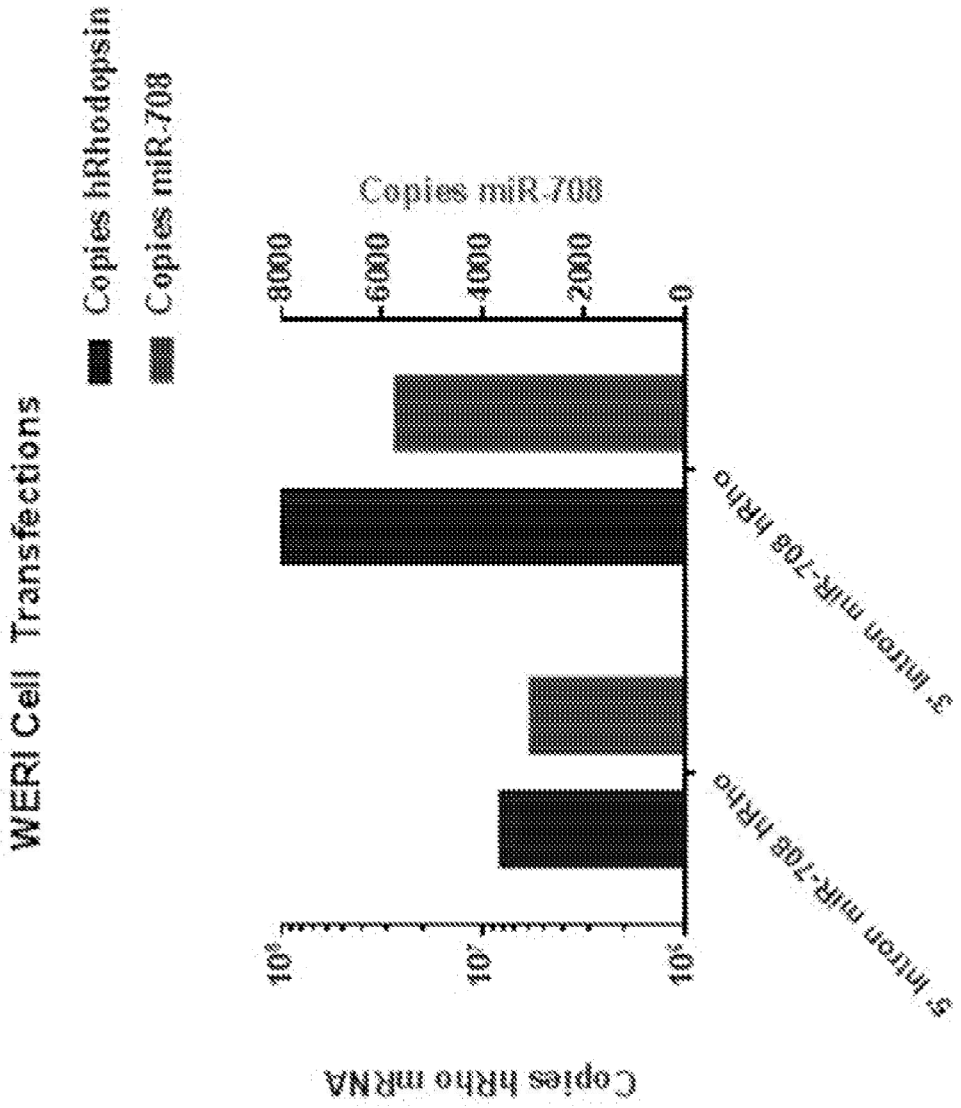

WERI Cell Transfections
Copies hRhodopsin
Copies miR-708
Copies miR-708
8000
6000
4000
2000
0
Copies hRho mRNA
10⁸
10⁷
10⁶
5' Intron miR-708 hRho
3' Intron miR-708 hRho

FIG. 18

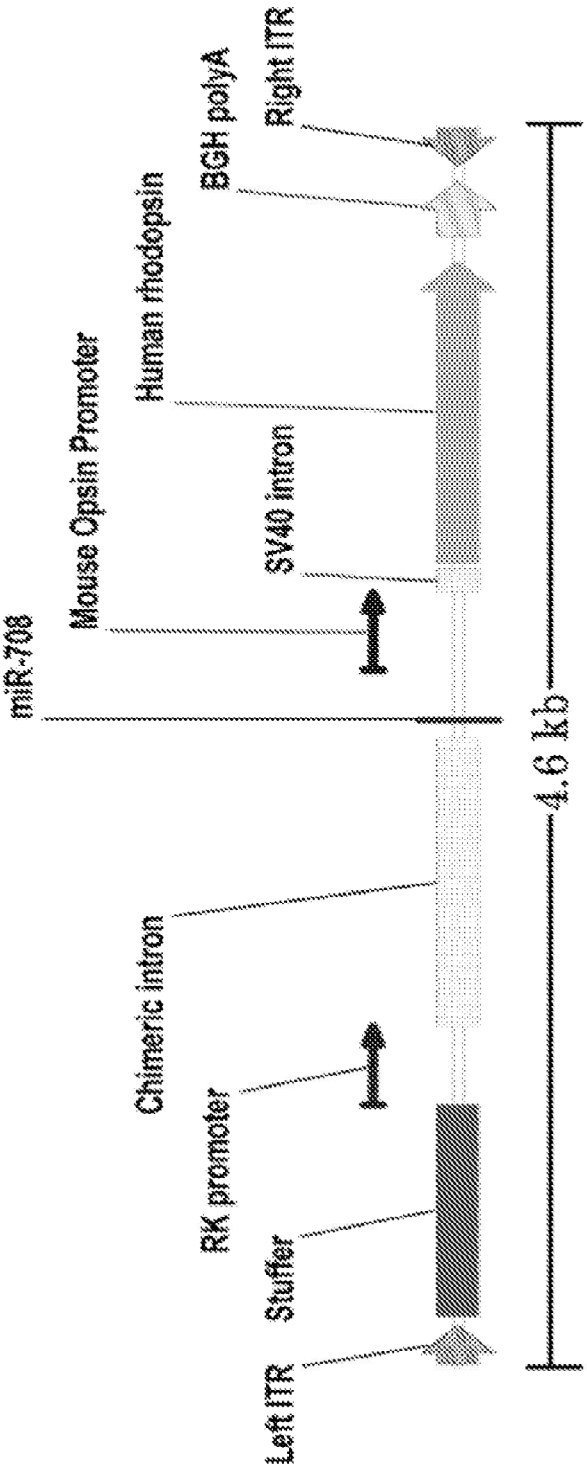

Left ITR
Stuffer
RK promoter
Chimeric intron
miR-708
Mouse Opsin Promoter
SV40 intron
Human rhodopsin
BGH polyA
Right ITR
4.6 kb

FIG. 19

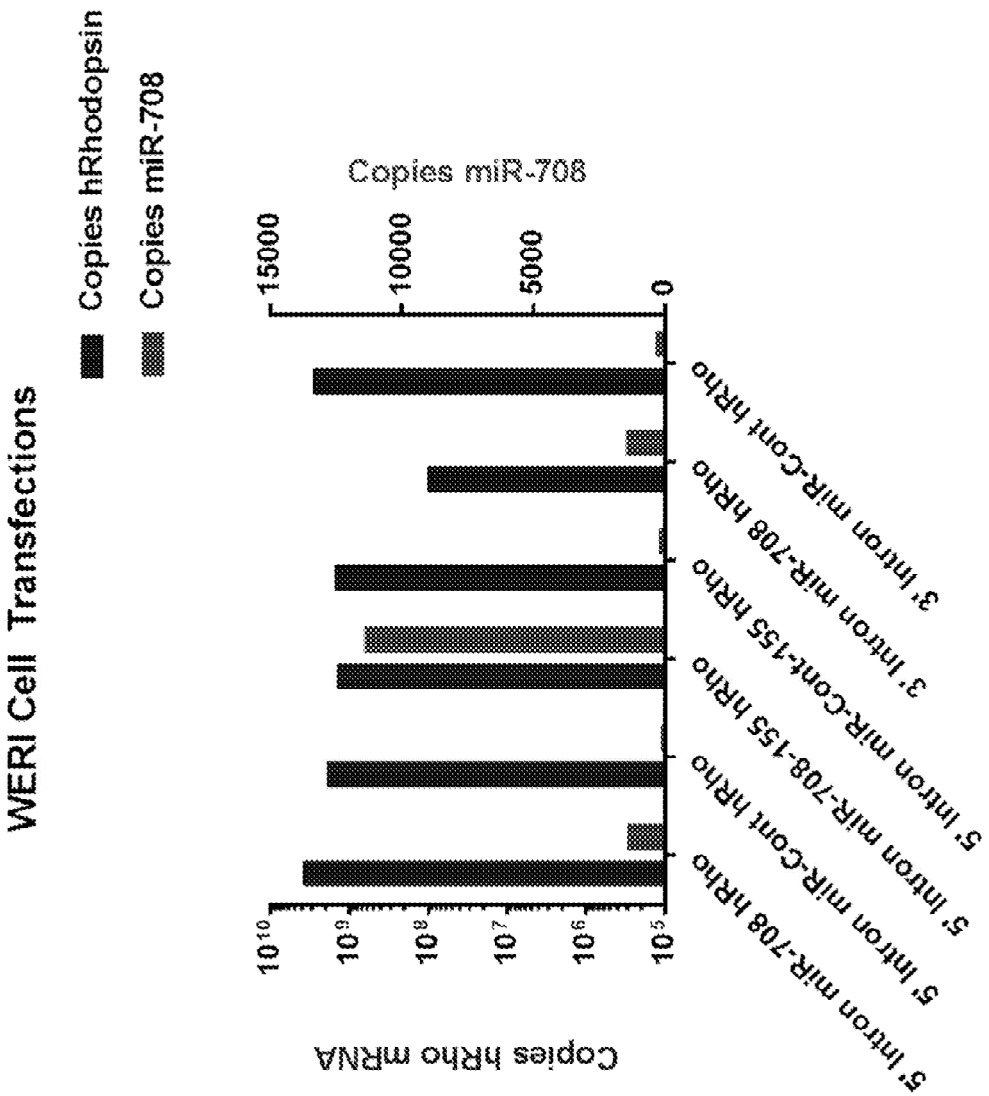

WERI Cell Transfections
Copies hRhodopsin
Copies miR-708
Copies miR-708
15000
10000
5000
0
Copies hRho mRNA
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
5' Intron miR-708 hRho
5' Intron miR-Cont hRho
5' Intron miR-708-155 hRho
5' Intron miR-Cont-155 hRho
3' Intron miR-708 hRho
3' Intron miR-Cont hRho

FIG. 20

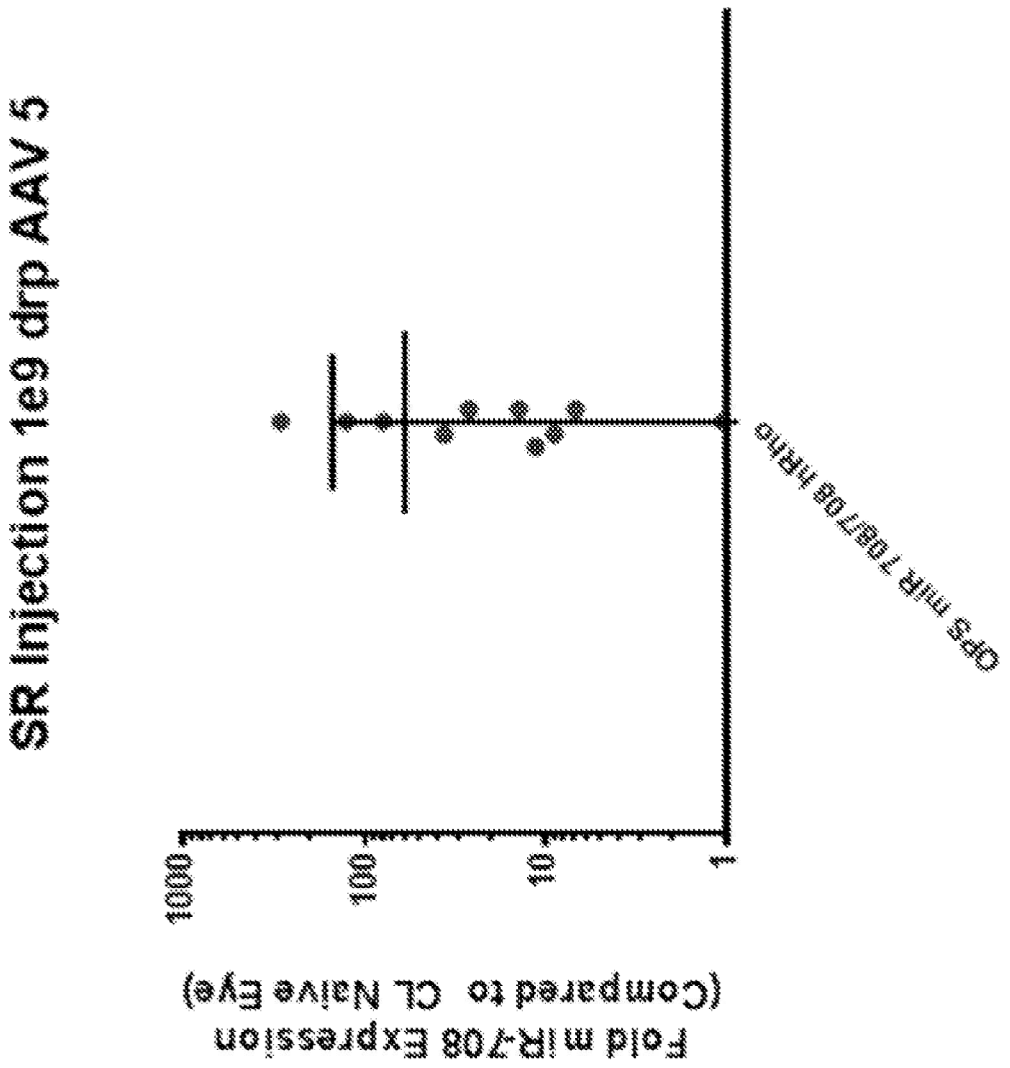

SR Injection 1e9 drp AAV 5
Fold miR-708 Expression
(Compared to CL Naive Eye)
1000
100
10
1
OPS miR 708/708 hRho

FIG. 21A

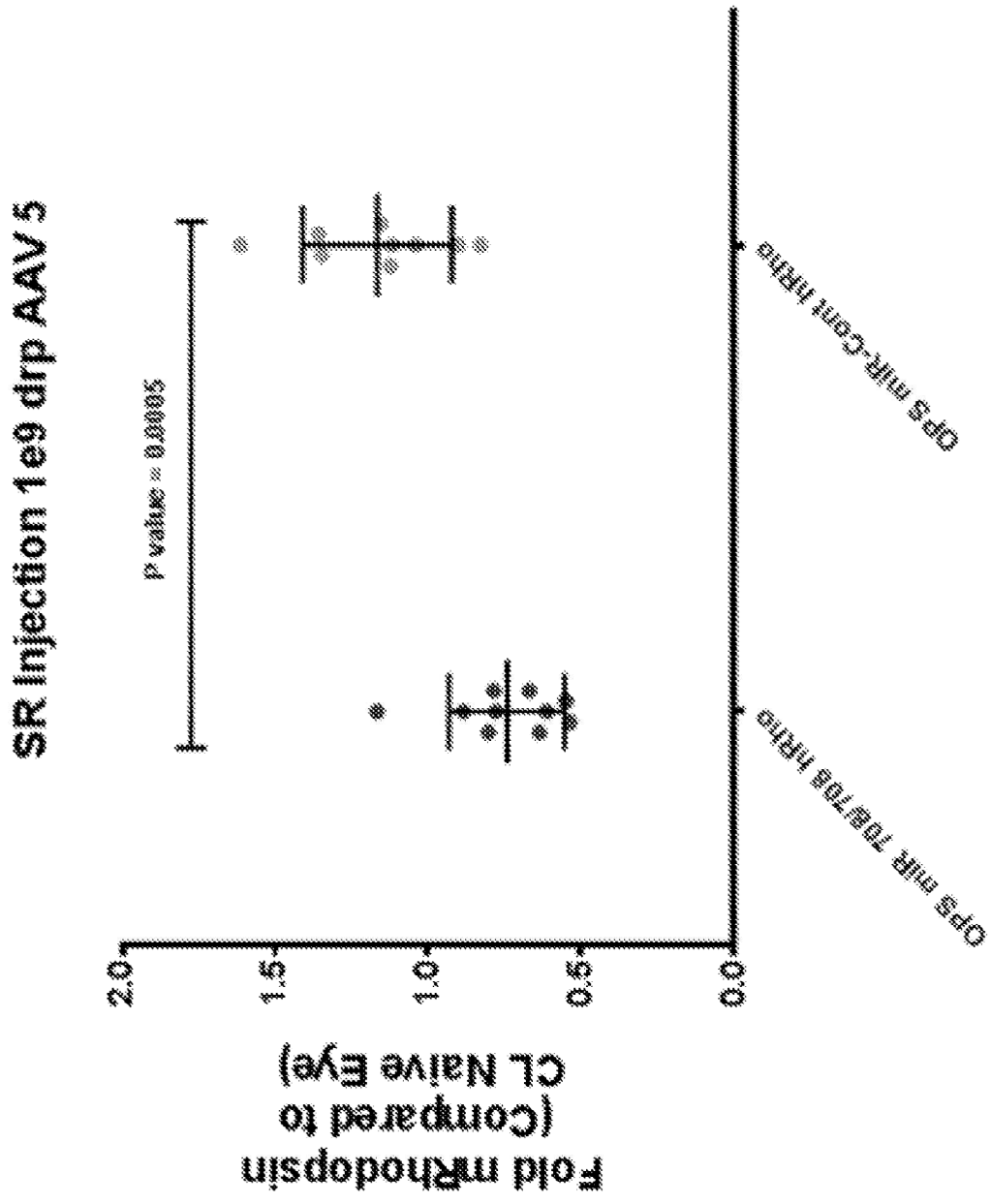

SR Injection 1e9 drp AAV 5
P value = 0.00005
Fold mRhodopsin
(Compared to
CL Naive Eye)
2.0
1.5
1.0
0.5
0.0
OPS mIR 708/708 hRho
OPS mIR-Coni hRho

FIG. 21B

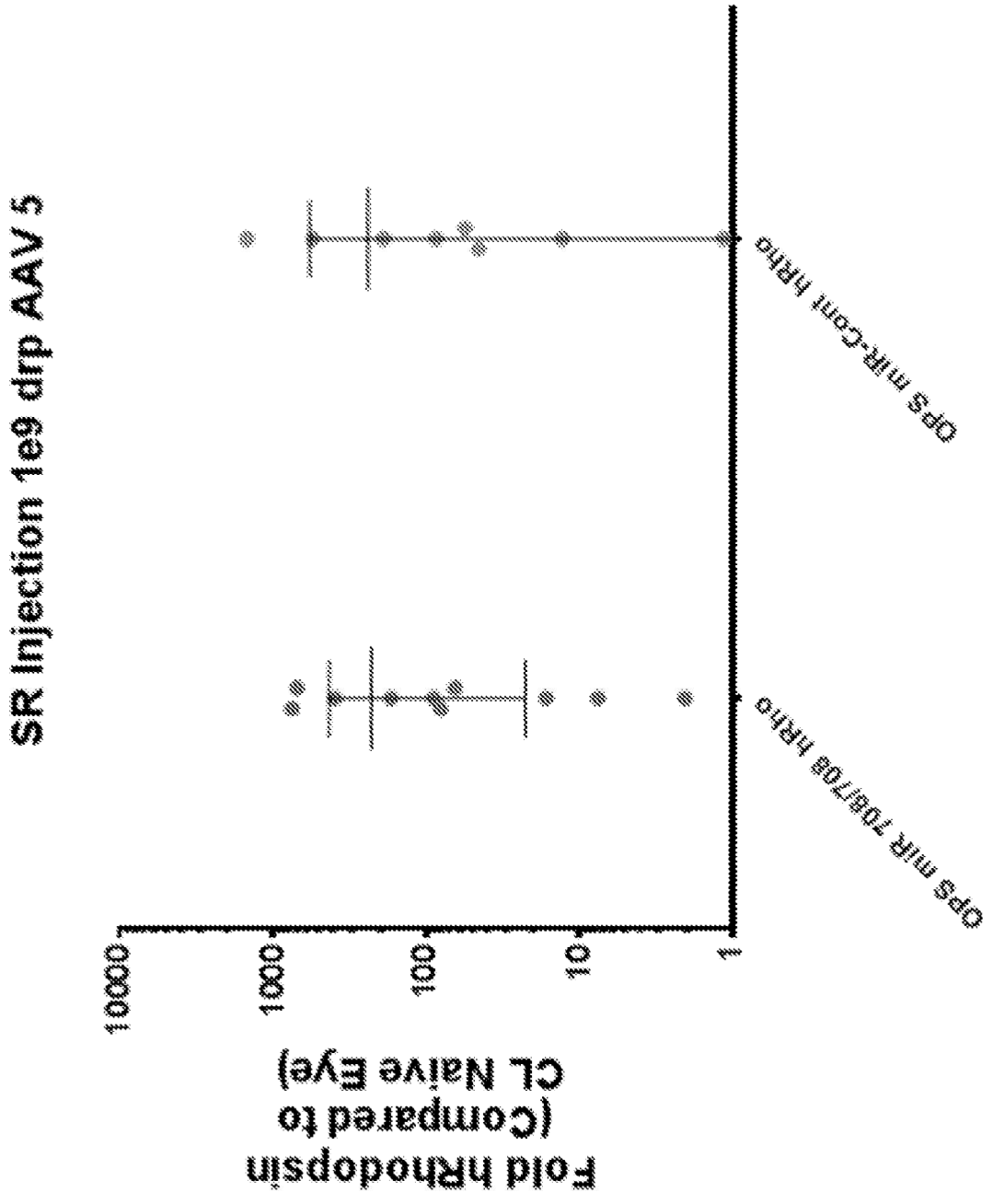

SR Injection 1e9 drp AAV 5
Fold hRhodopsin
(Compared to
cL Naive Eye)
10000
1000
100
10
1
OPS mIR 708/708 hRho
OPS mIR-Coni hRho

FIG. 21C

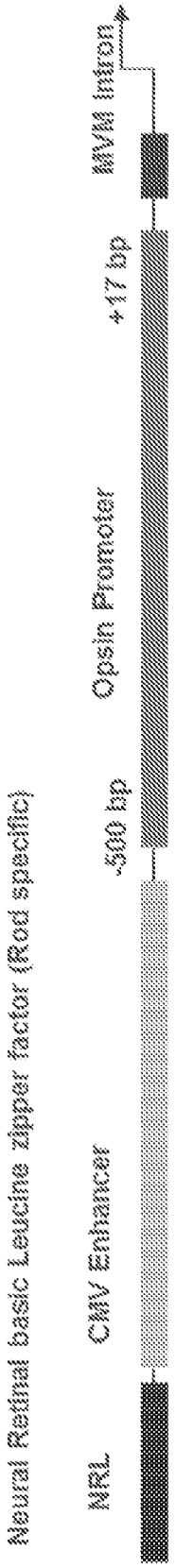

Neural Retinal basic Leucine zipper factor (Rod specific)
NRL
65 bp
CMV Enhancer
400 bp
-500 bp
Opsin Promoter
+17 bp
MVM intron

FIG. 22

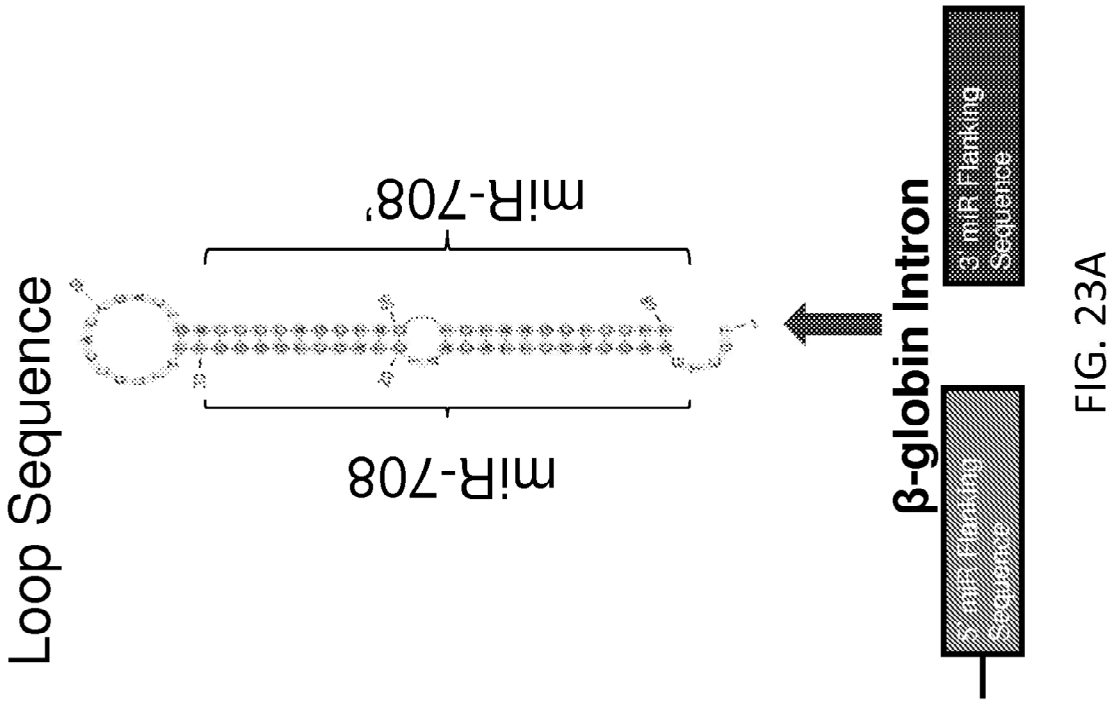
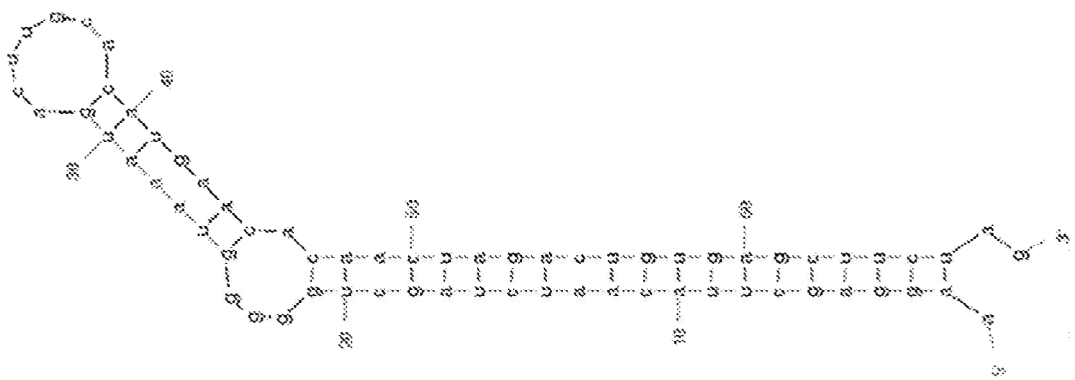

5' miR Flanking Sequence
β-globin Intron
3' miR Flanking Sequence
miR-708
miR-708'
Loop Sequence

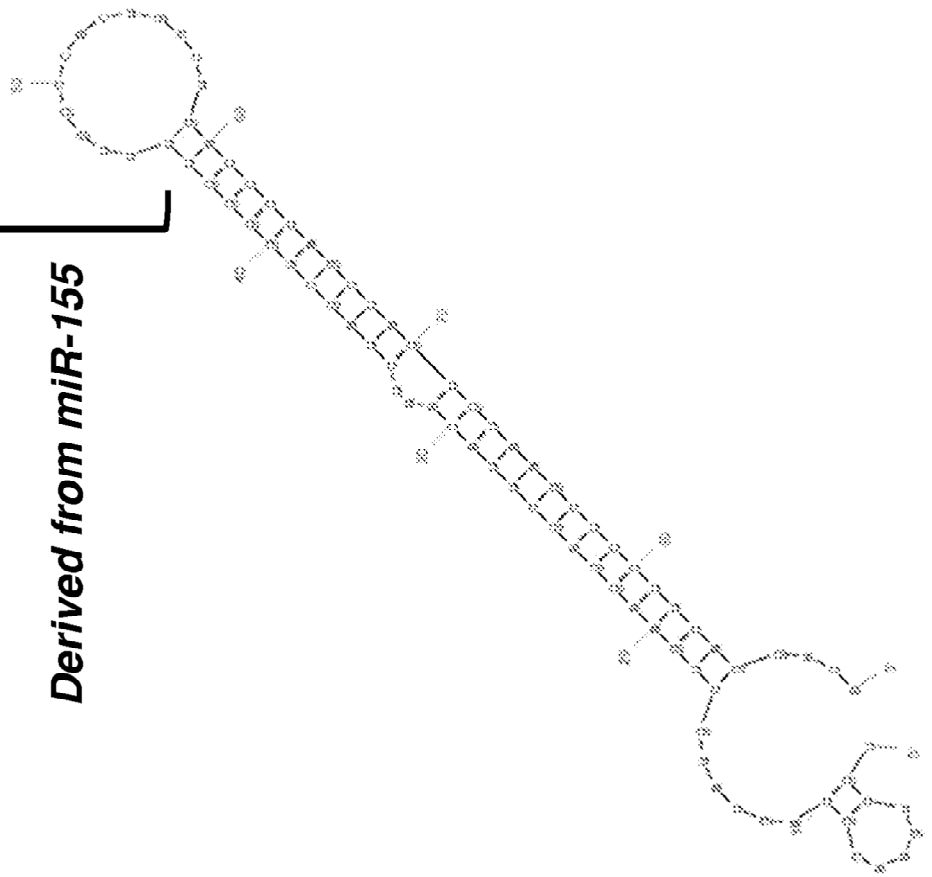
FIG. 23A

FIG. 23B



miR-708

FIG. 23C



miR-155

Derived from miR-155

FIGS. 23B & 23C

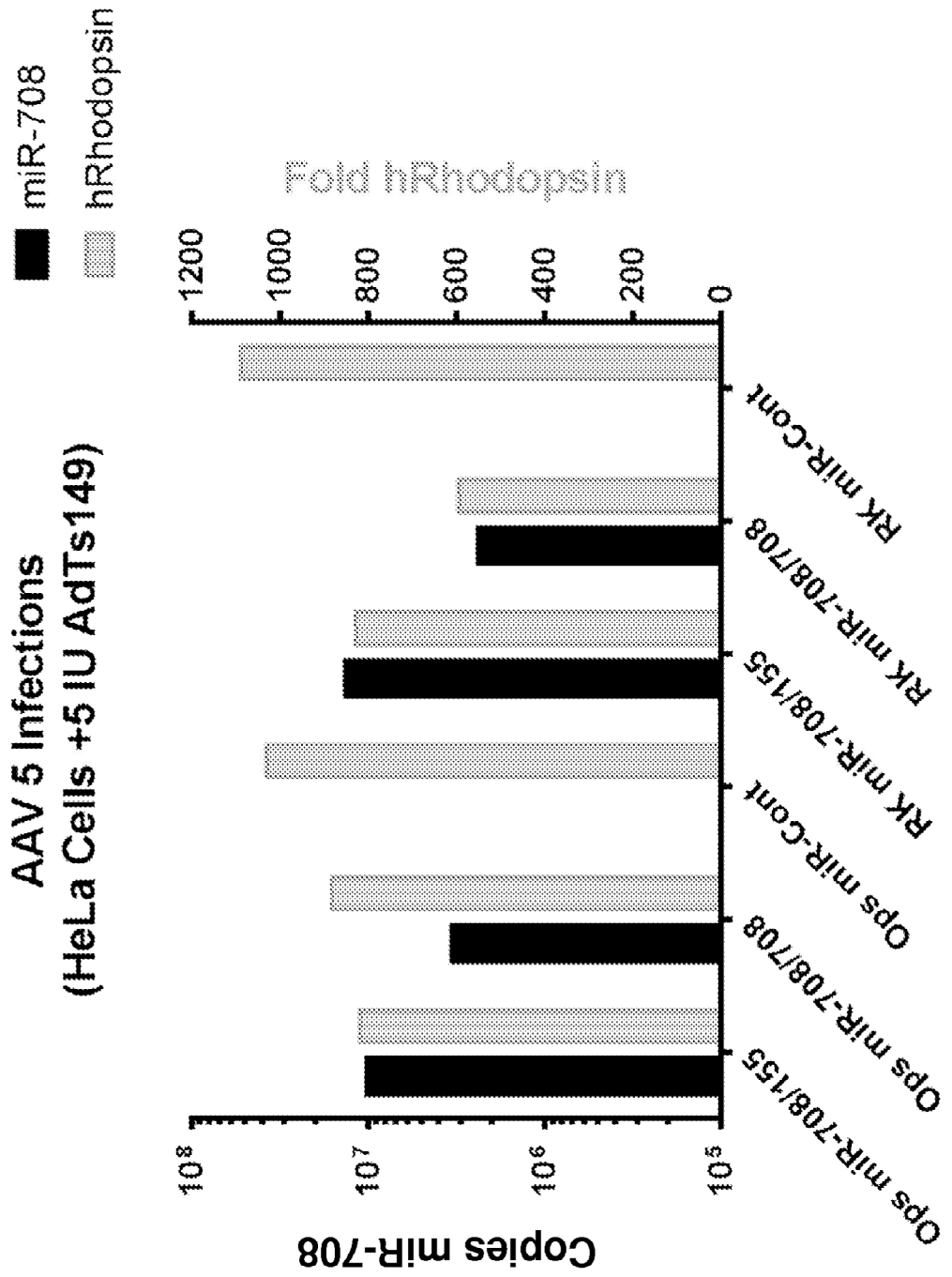

AAV 5 Infections
(HeLa Cells +5 IU AdTs149)
miR-708
hRhodopsin
Fold hRhodopsin
1200
1000
800
600
400
200
0
Copies miR-708
10^8
10^7
10^6
10^5
Ops miR-708/155
Ops miR-708/708
Ops miR-Cont
RK miR-708/155
RK miR-708/708
RK miR-Cont

FIG. 24