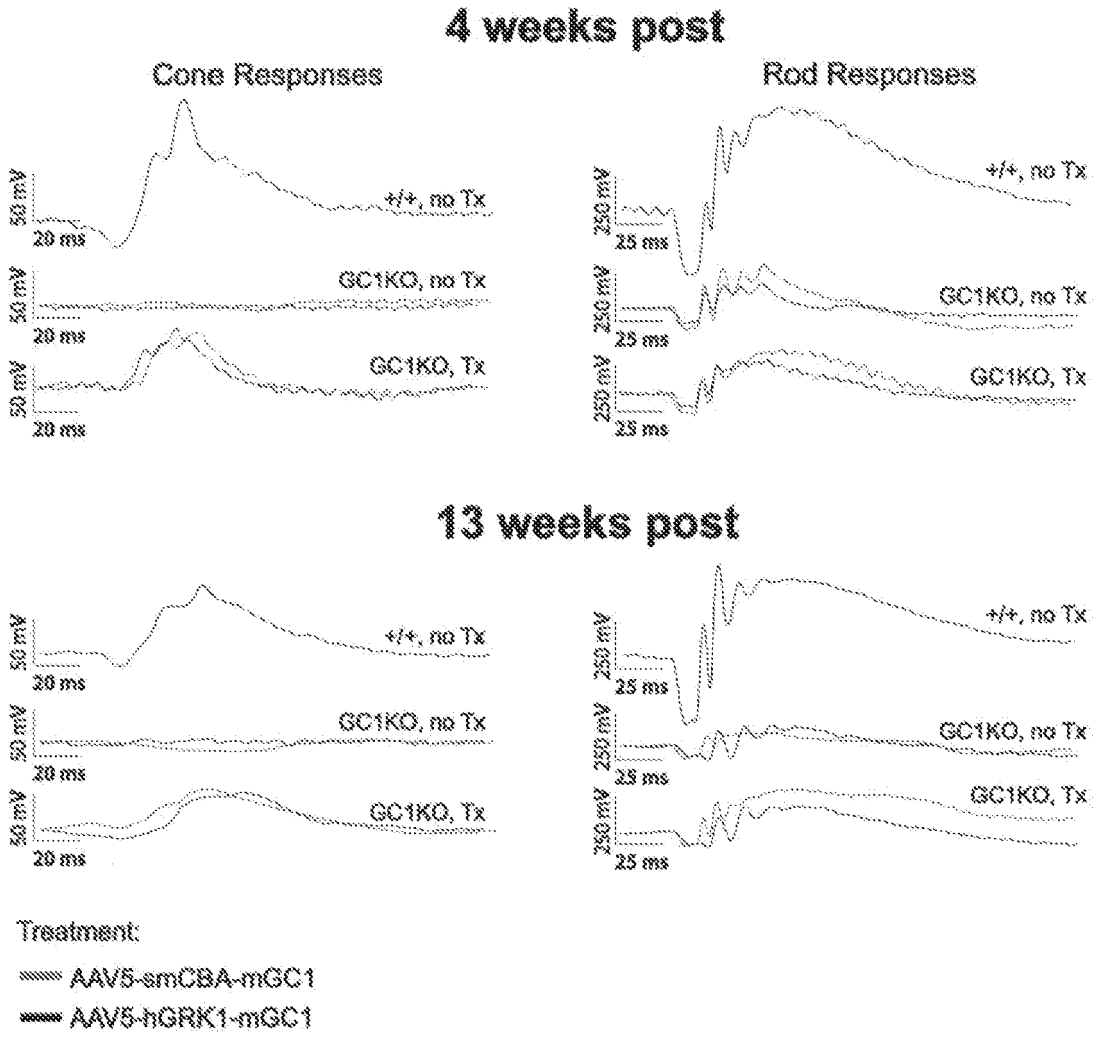

4 weeks post
Cone Responses
Rod Responses
+/+, no Tx
GC1KO, no Tx
GC1KO, Tx
50 mV
20 ms
250 mV
25 ms
13 weeks post
Treatment:
AAV5-smCBA-mGC1
AAV5-hGRK1-mGC1

FIG. 1

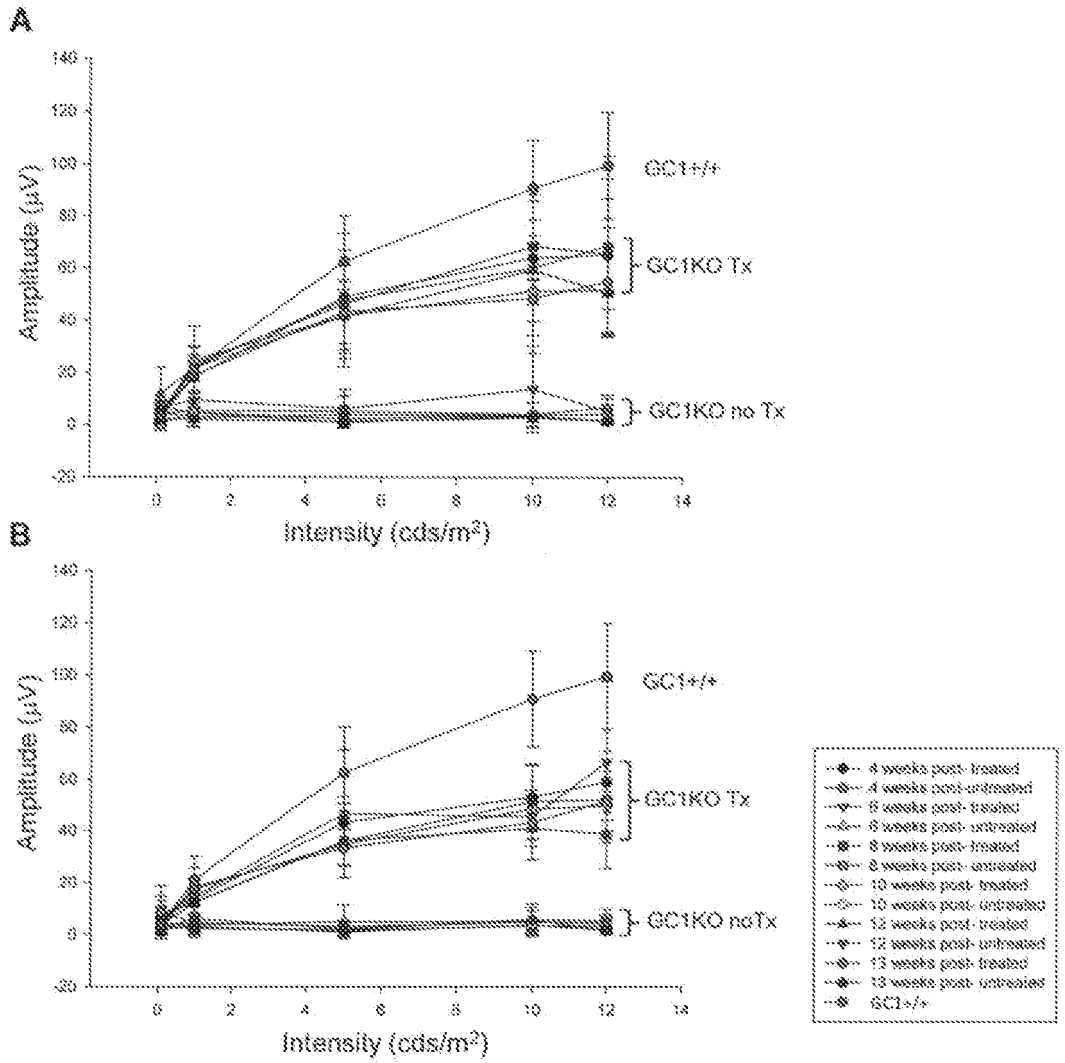

A
Amplitude (μV)
Intensity (cds/m²)
GC1+/+
GC1KO Tx
GC1KO no Tx
B
Amplitude (μV)
Intensity (cds/m²)
GC1+/+
GC1KO Tx
GC1KO noTx
4 weeks post- treated
4 weeks post- untreated
6 weeks post- treated
6 weeks post- untreated
8 weeks post- treated
8 weeks post- untreated
10 weeks post- treated
10 weeks post- untreated
12 weeks post- treated
12 weeks post- untreated
13 weeks post- treated
13 weeks post- untreated
GC1+/+

FIG. 2A and 2B

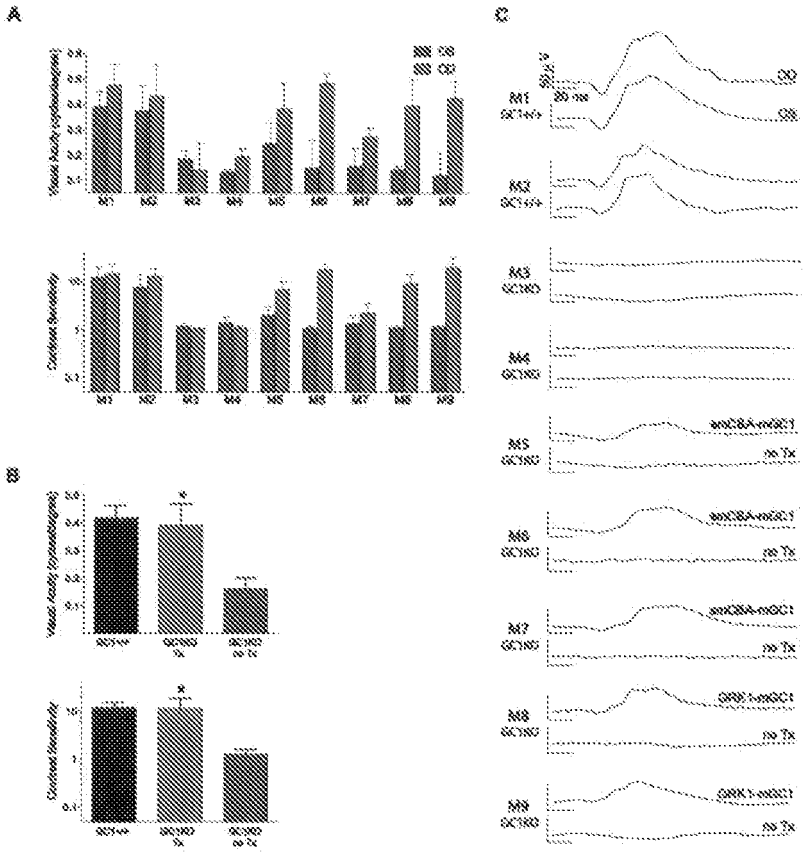


FIG. 3A, FIG. 3B, and FIG. 3C

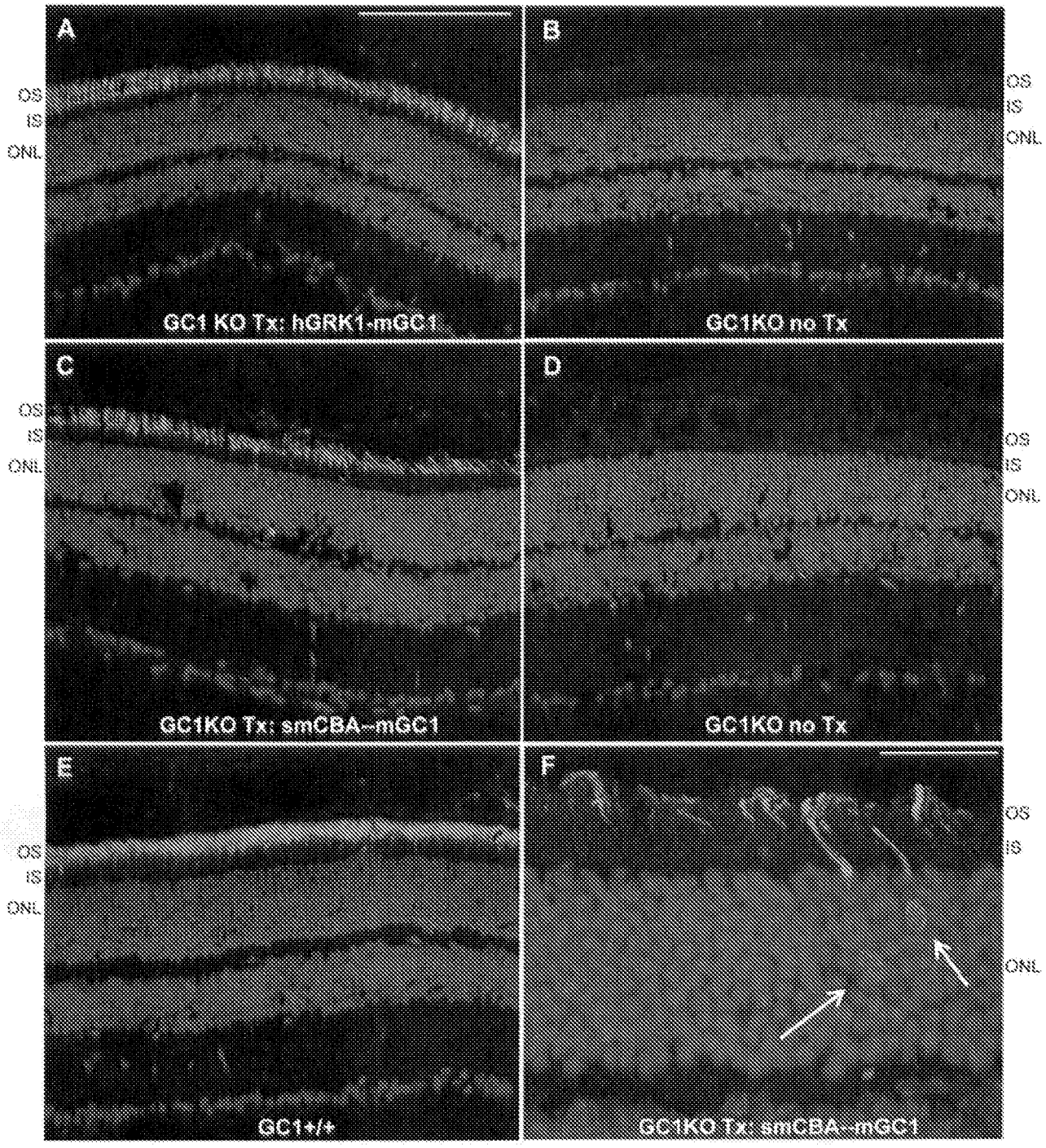


FIG. 4A, FIG. 4B, FIG. 4C, FIG. D, and FIG. F

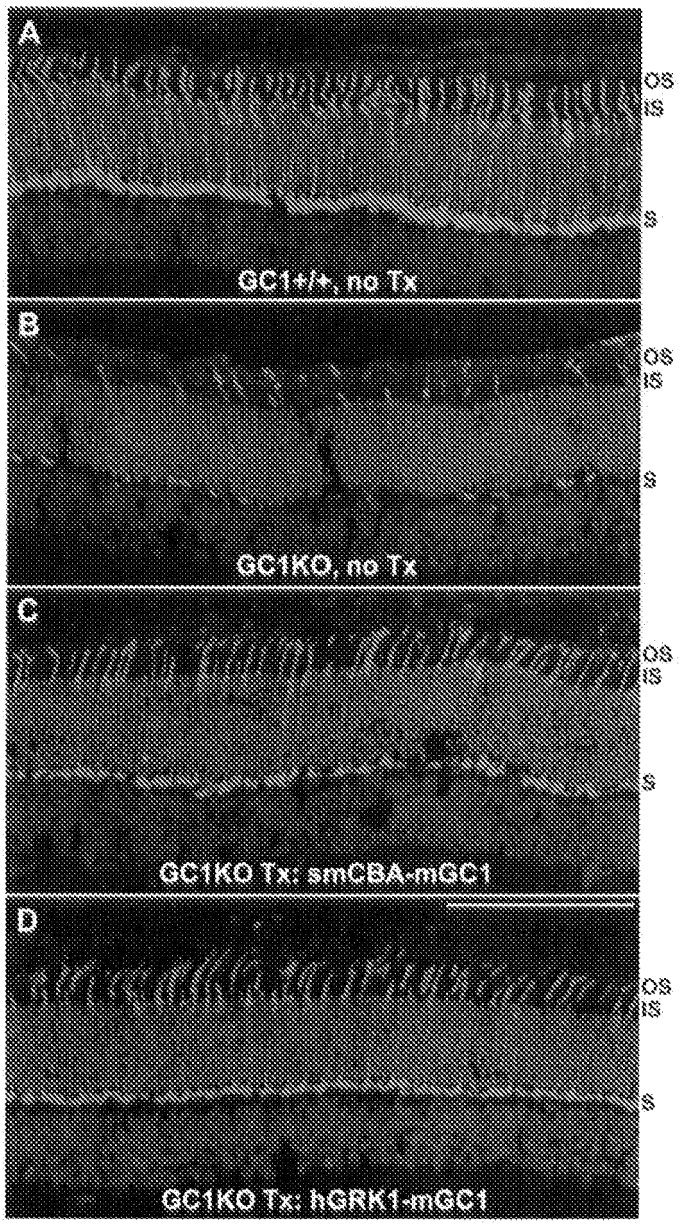


FIG. 5A, FIG. 5B, FIG. 5C and FIG. 5D

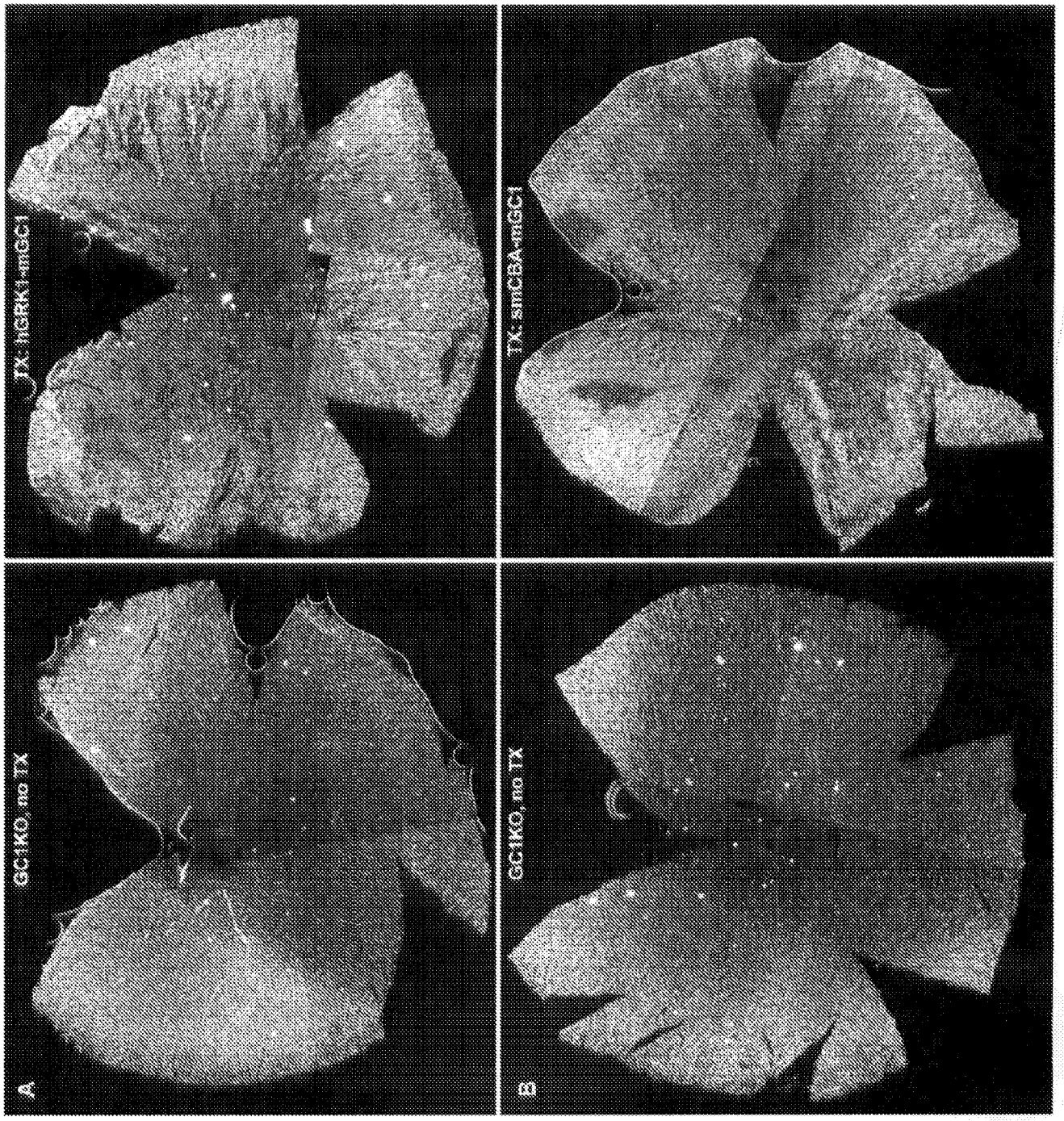


FIG. 6A, FIG. 6B, FIG. 6C and FIG. 6D

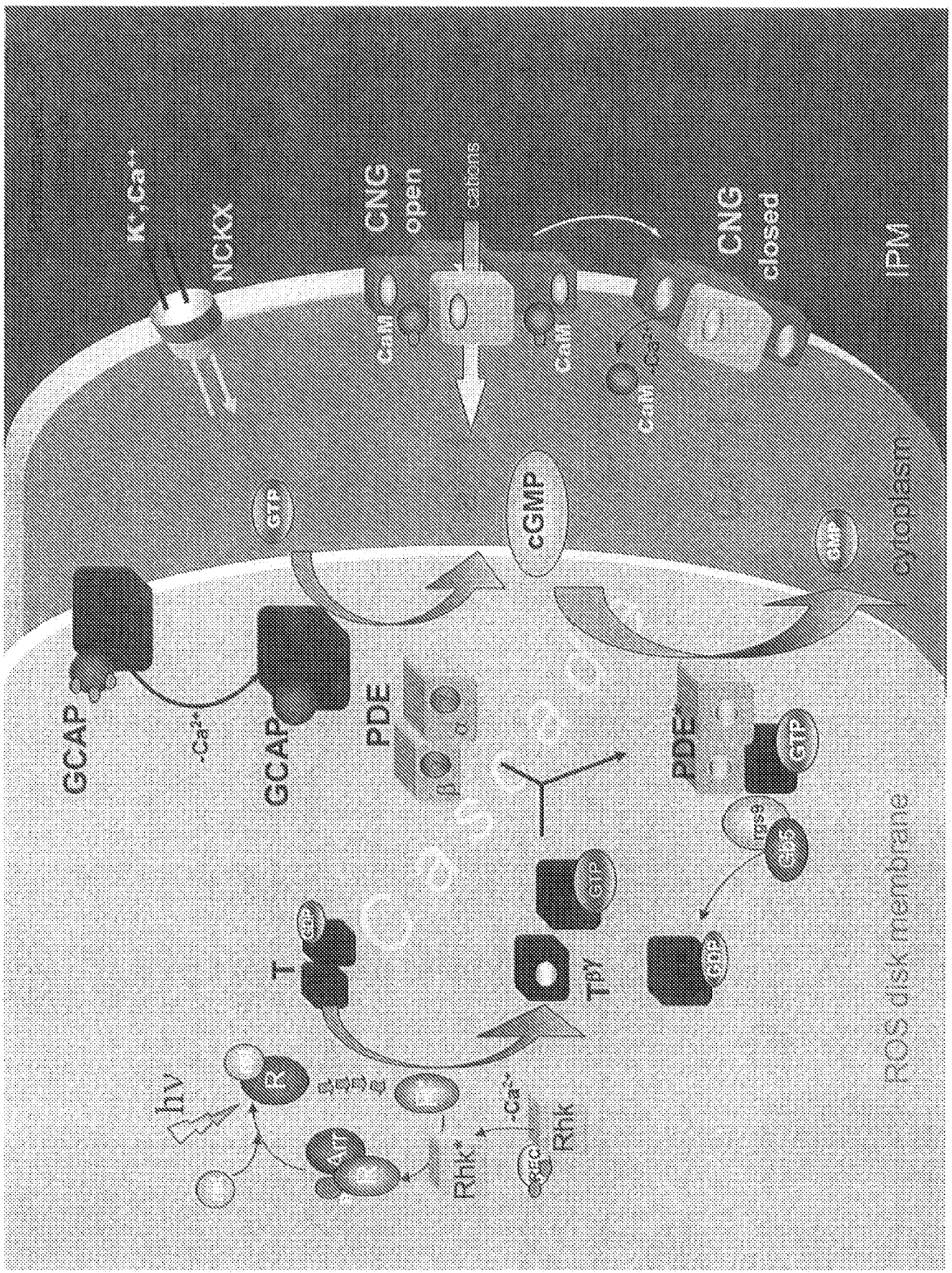

K+,Ca++
NCKX
CNG
open
cations
CNG
closed
IPM
cytoplasm
ROS disk membrane
GCAP
GCAP
PDE
cGMP
GMP
GTP
hν
Rhk*
Rhk
T
Tβγ
PDE*
PDE

FIG. 7

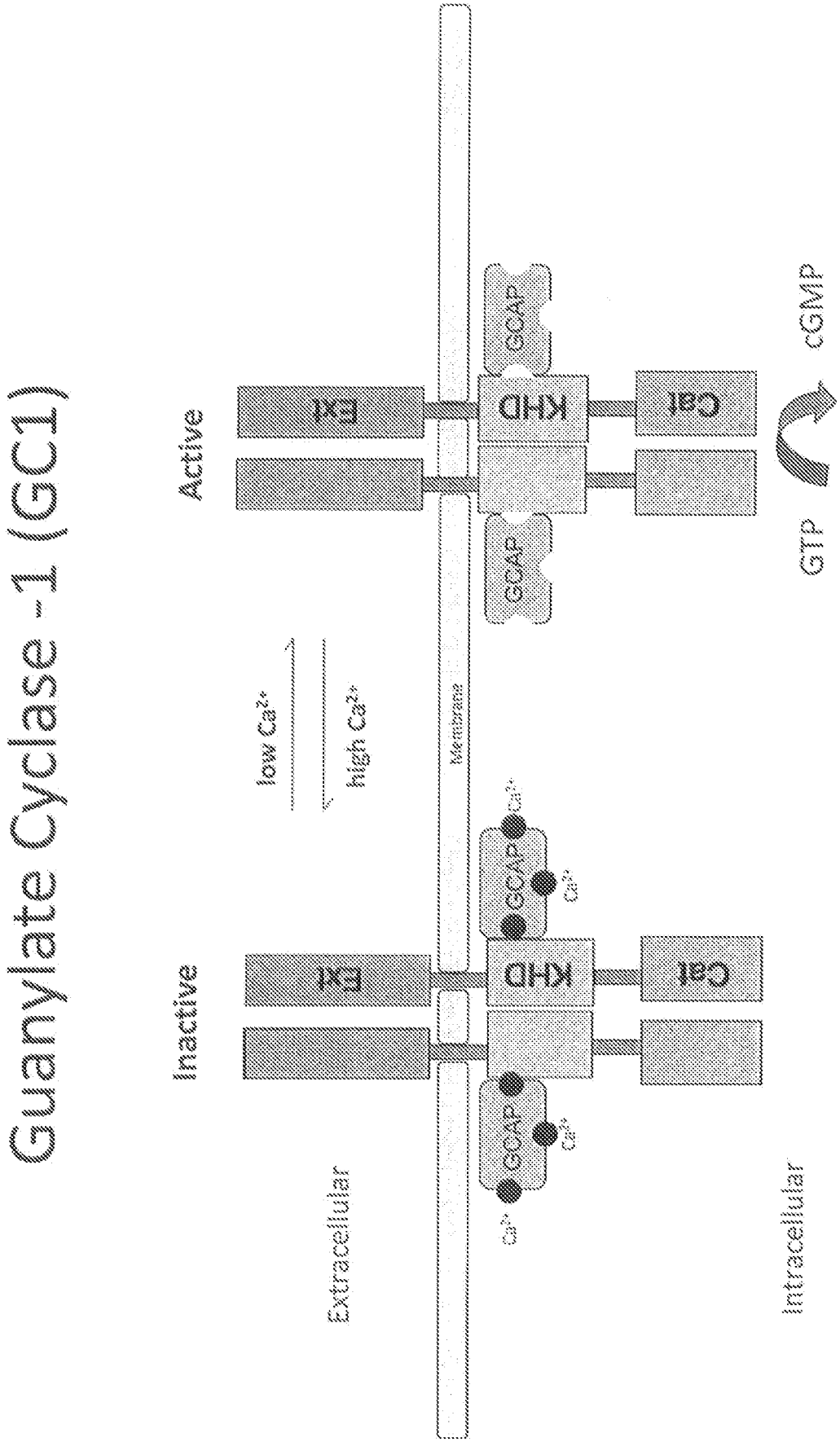

Guanylate Cyclase -1 (GC1)
Active
Inactive
Ext
KHD
Cat
GCAP
GTP
cGMP
low Ca2+
high Ca2+
Membrane
Extracellular
Intracellular
Ca2+

FIG. 8

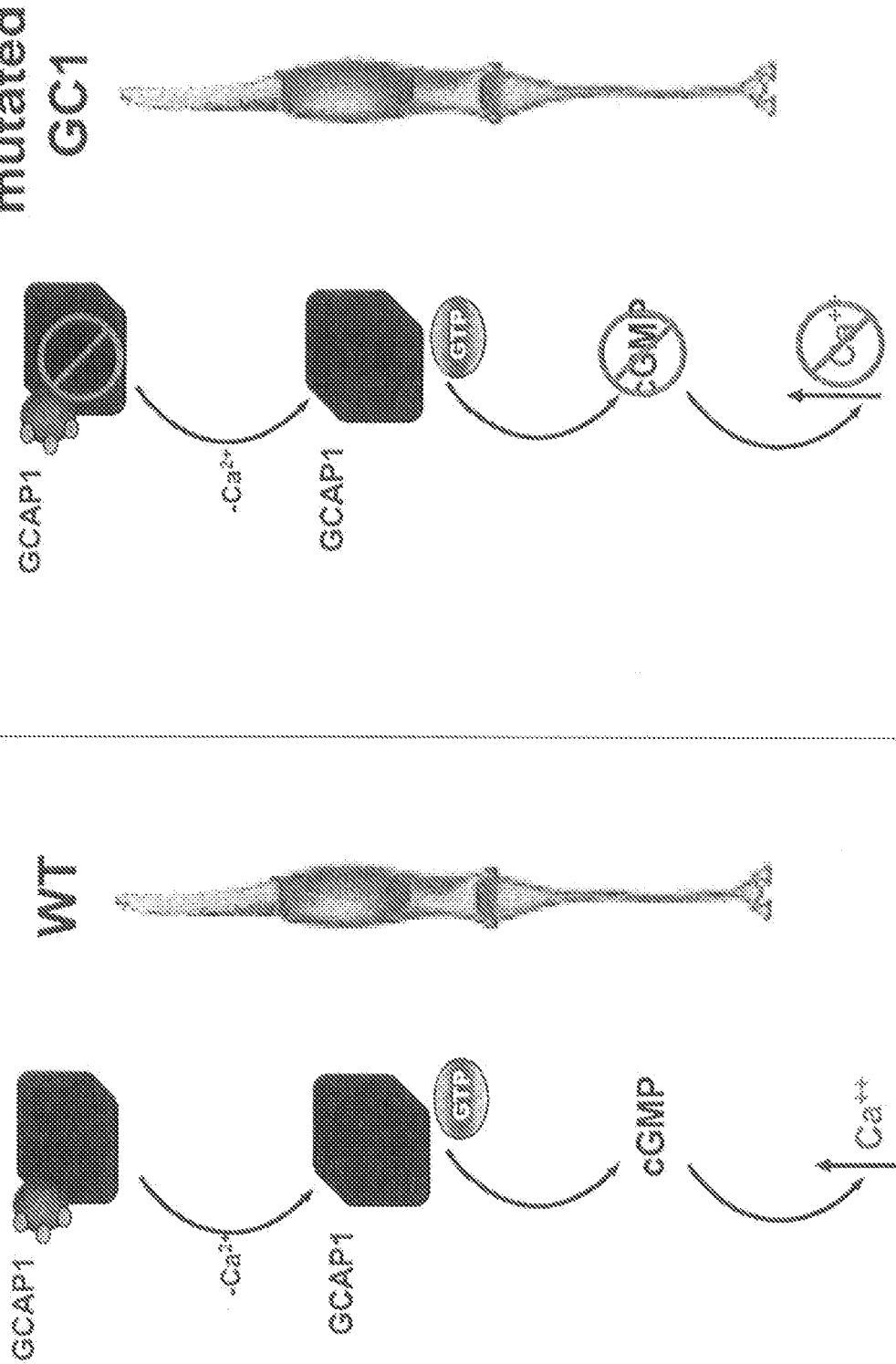

mutated
GC1
GCAP1
-Ca2+
GCAP1
GTP
cGMP
Ca2+
•Do NOT transduce light for vision
•Do degenerate
•Chronically hyperpolarized- "Locked into" artificial state of constant light stimulation
WT
GCAP1
-Ca2+
GCAP1
GTP
cGMP
Ca2+
•Transduce light for vision normally
•Do NOT degenerate

FIG. 9

FIG. 10

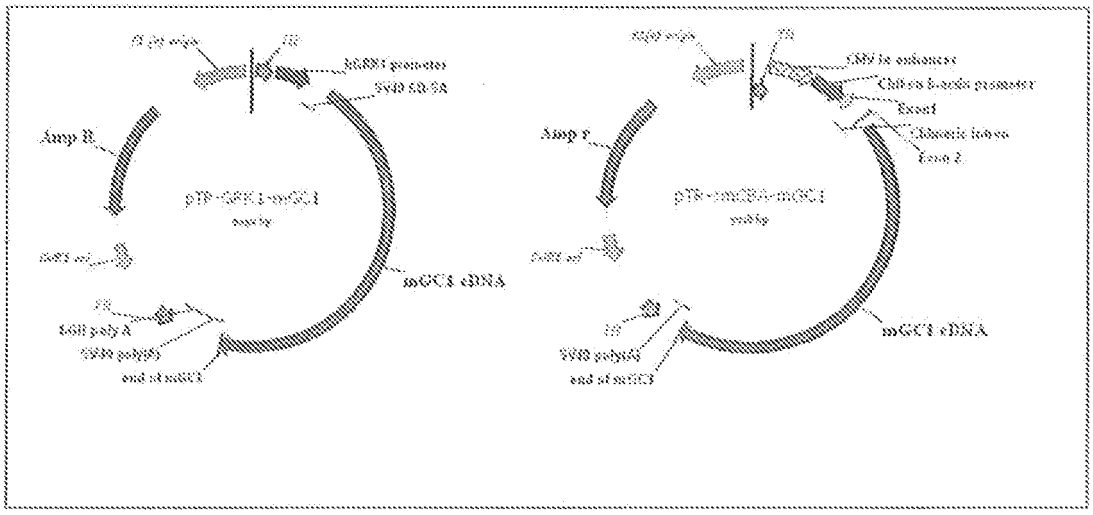


FIG. 11

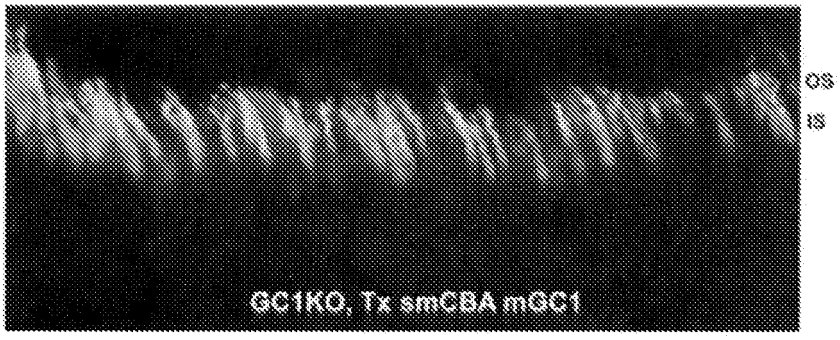


FIG. 12

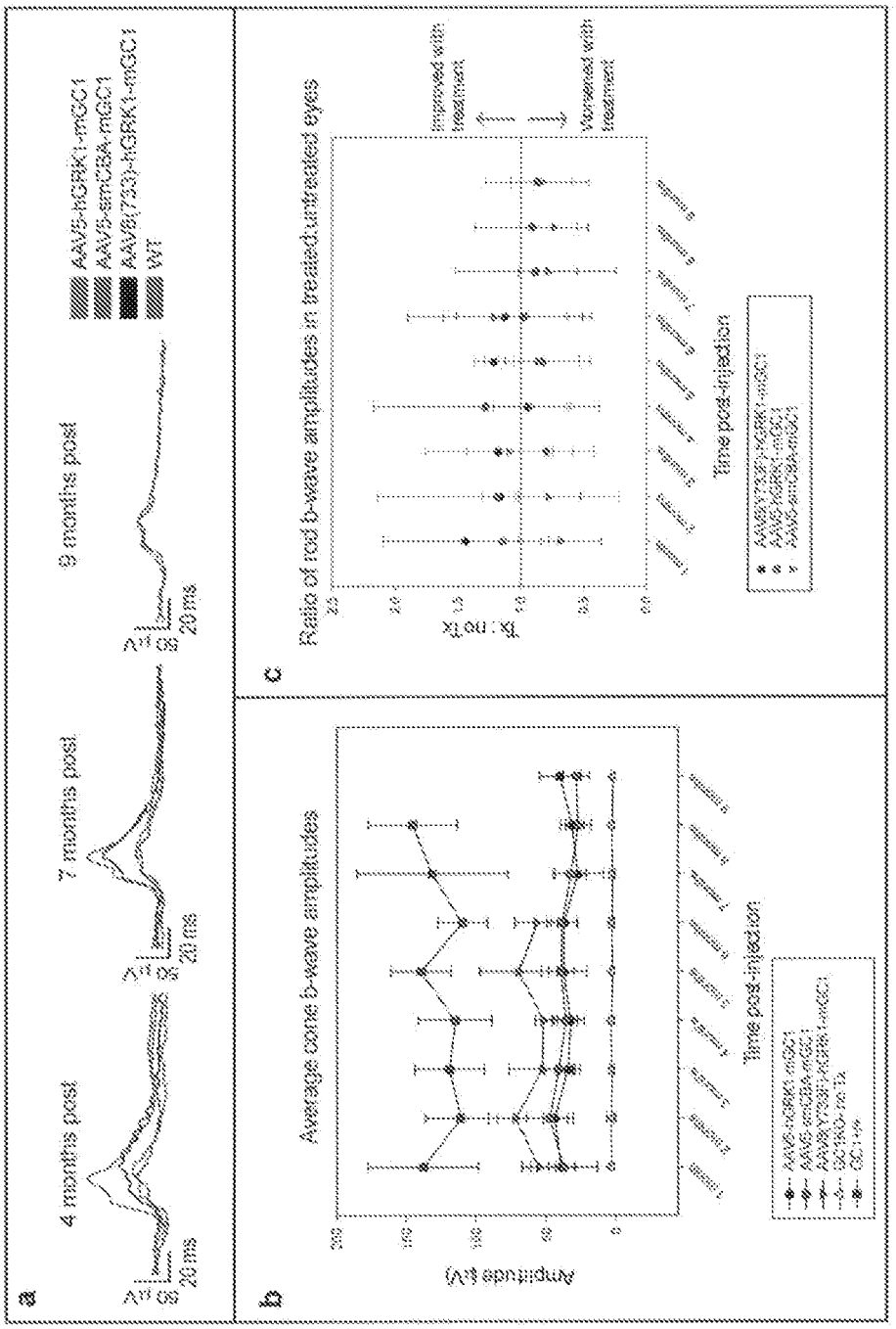


FIG. 13A, FIG. 13B, and FIG. 13C

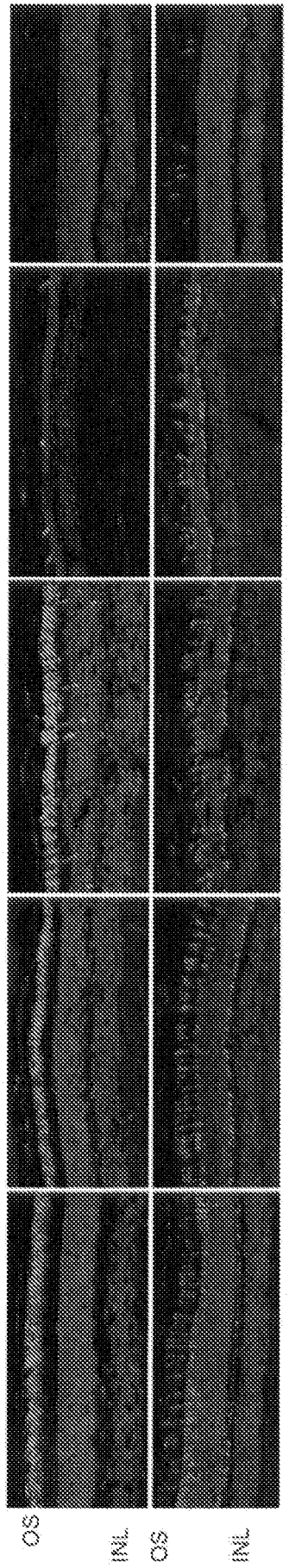

GC1+/+
AAV8(733)-hGRK1-mGC1
AAV8-mCBA-mGC1
AAV8-hGRK1-mGC1
GC1KO- no Tx
OS
INL
OS
INL

FIG. 14

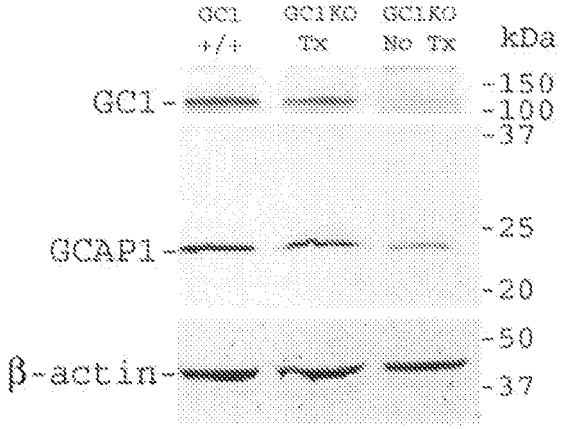

GC1 +/+
GC1KO Tx
GC1KO No Tx
kDa
GC1
GCAP1
β-actin
150
100
37
25
20
50
37

FIG. 15

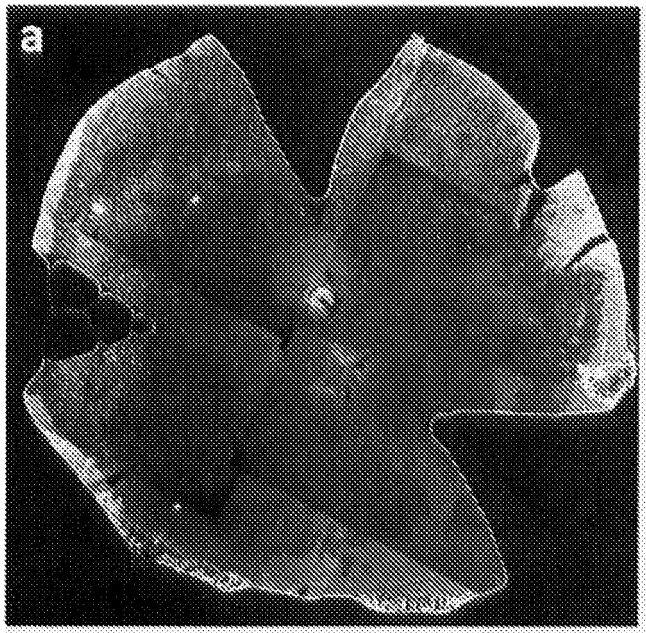


FIG. 16A

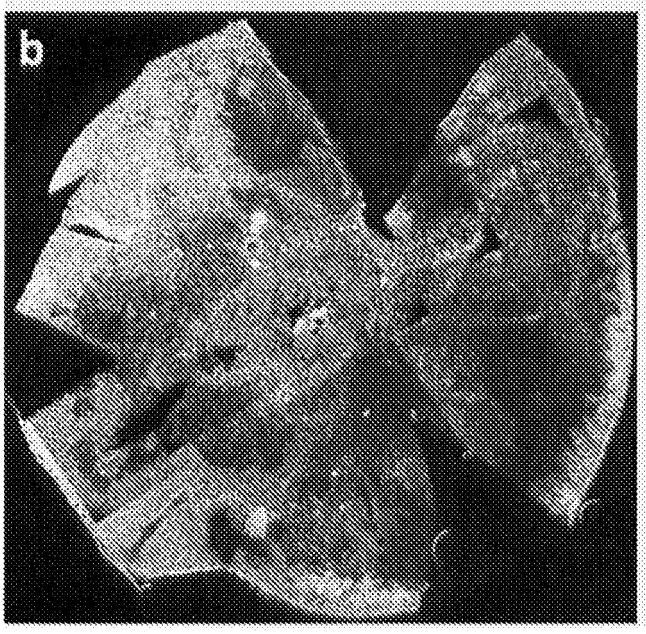


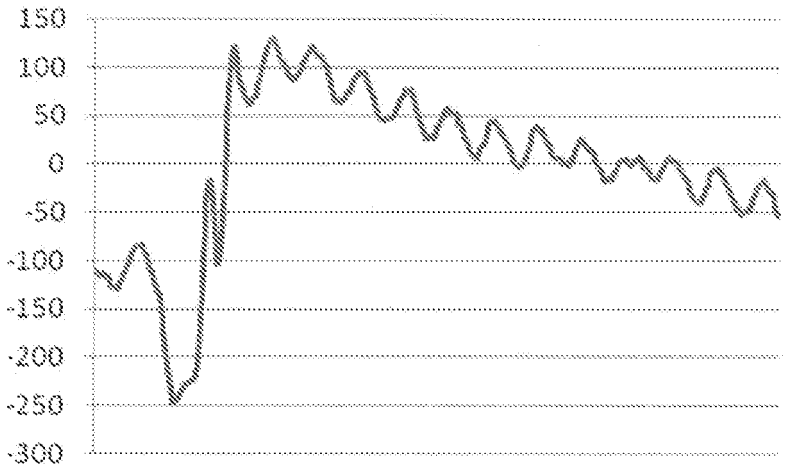
FIG. 16B

Detection of rAAV vector sequences by PCR in GC1KO tissue samples

	M1a	M2b	M3b	M4c	M5c	M6c	M7c	M8c	M9b	M10c	M11b	M12c
	AAV8(733)-hGRK1	AAV8(733)-hGRK1	AAV5-smCBA	AAV5-smCBA	AAV5-smCBA	AAV5-smCBA	AAV5-smCBA	AAV5-smCBA	AAV5-hGRK1	AAV5-hGRK1	no Tx	no Tx
Optic Nerve R	na	na	+160	+1000	+970	+1890	na	+395	+3140	+1695	-	-
Optic Nerve L	+632	+25,885	-	na	na	na	na	na	-	na	na	na
Brain R	-	-	-	-	-	-	-	-	-	-	-	-
Brain L	-	-	-	-	-	-	-	-	+252	-	-	-

M, Animal; R, right; L, left; Tx, treatment; -, no PCR amplification; +, PCR amplification of vector sequence (replicated value shown is average, copy number per mg of DNA; na, not available (not determinable because of an unacceptable spike-in)
a 4 months post injection
b 7 months post injection
c 10 months post injection

FIG. 17



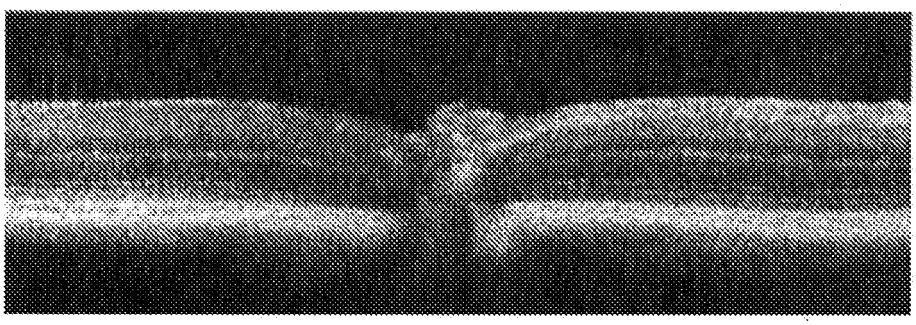


FIG. 18A

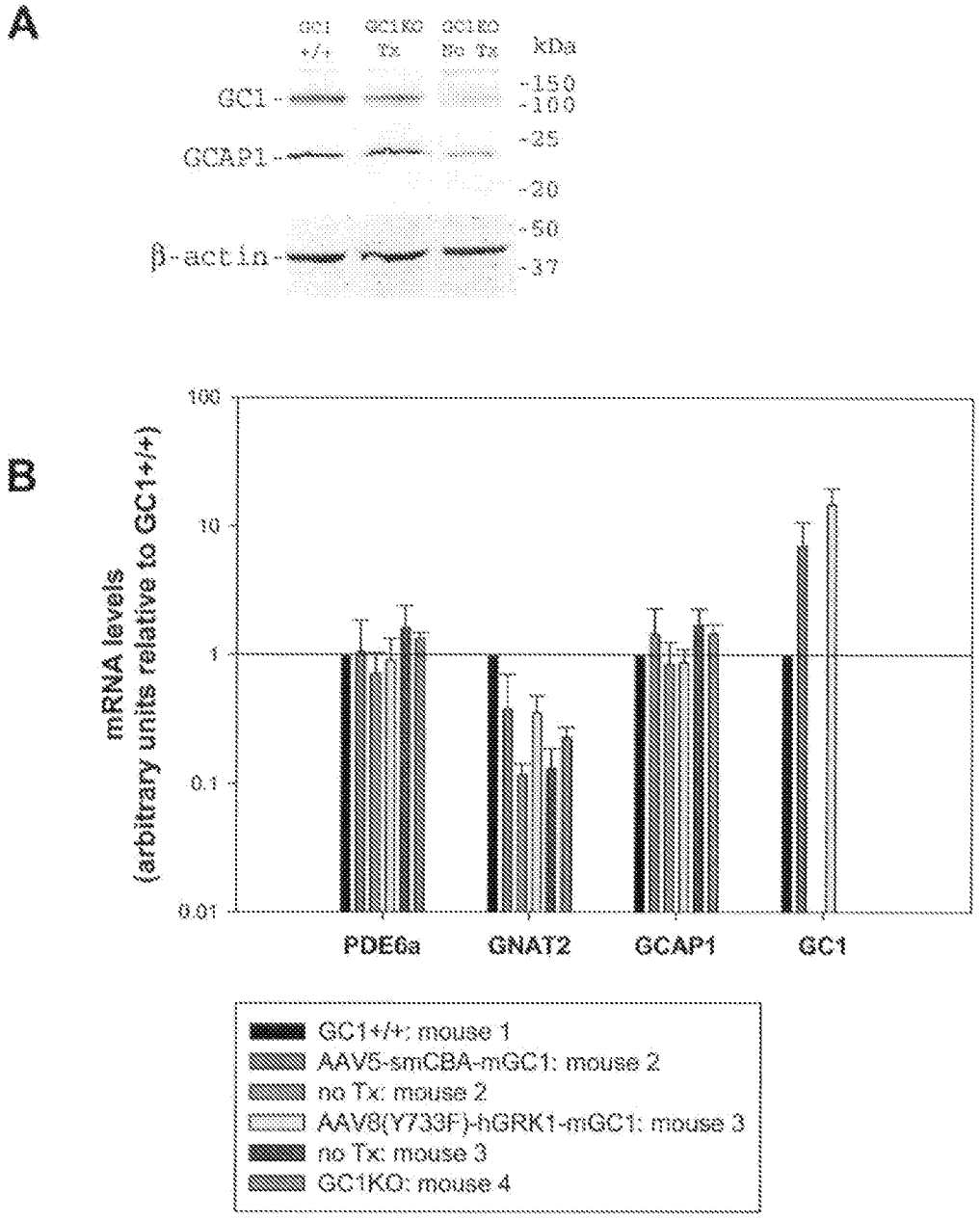
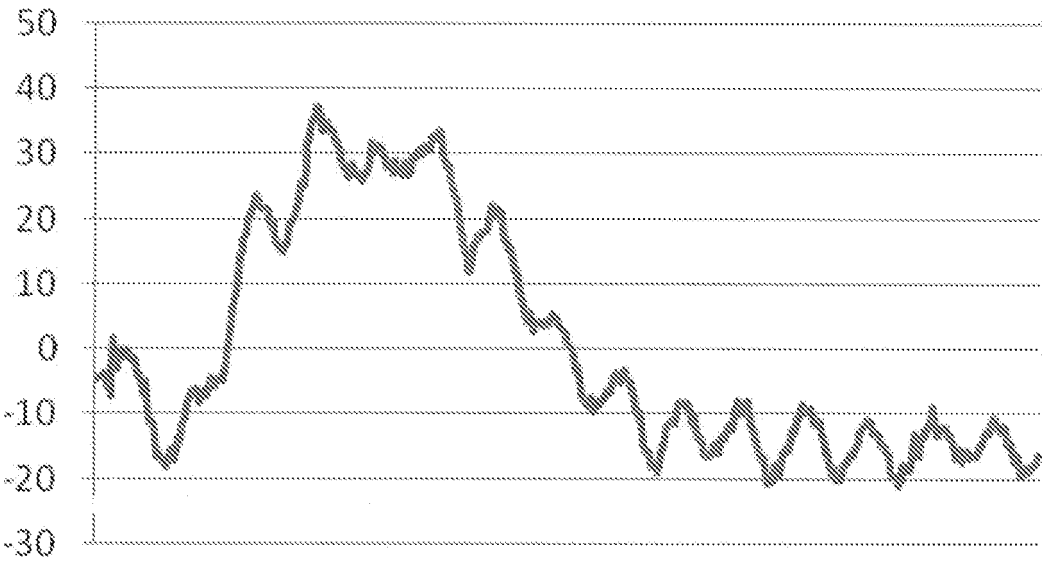


FIG. 20A and FIG. 20B



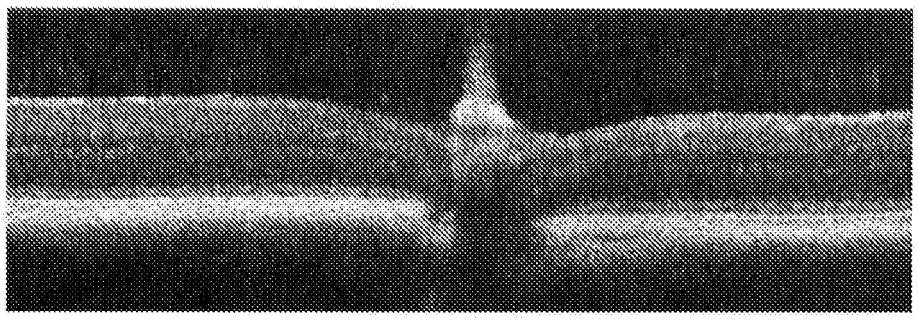


FIG. 18B

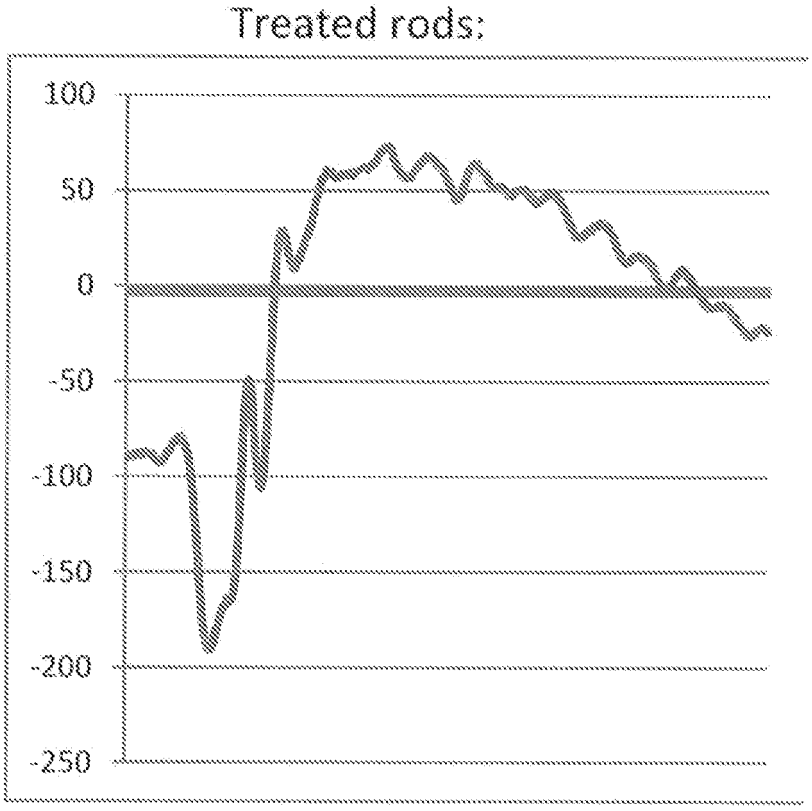


FIG. 19A

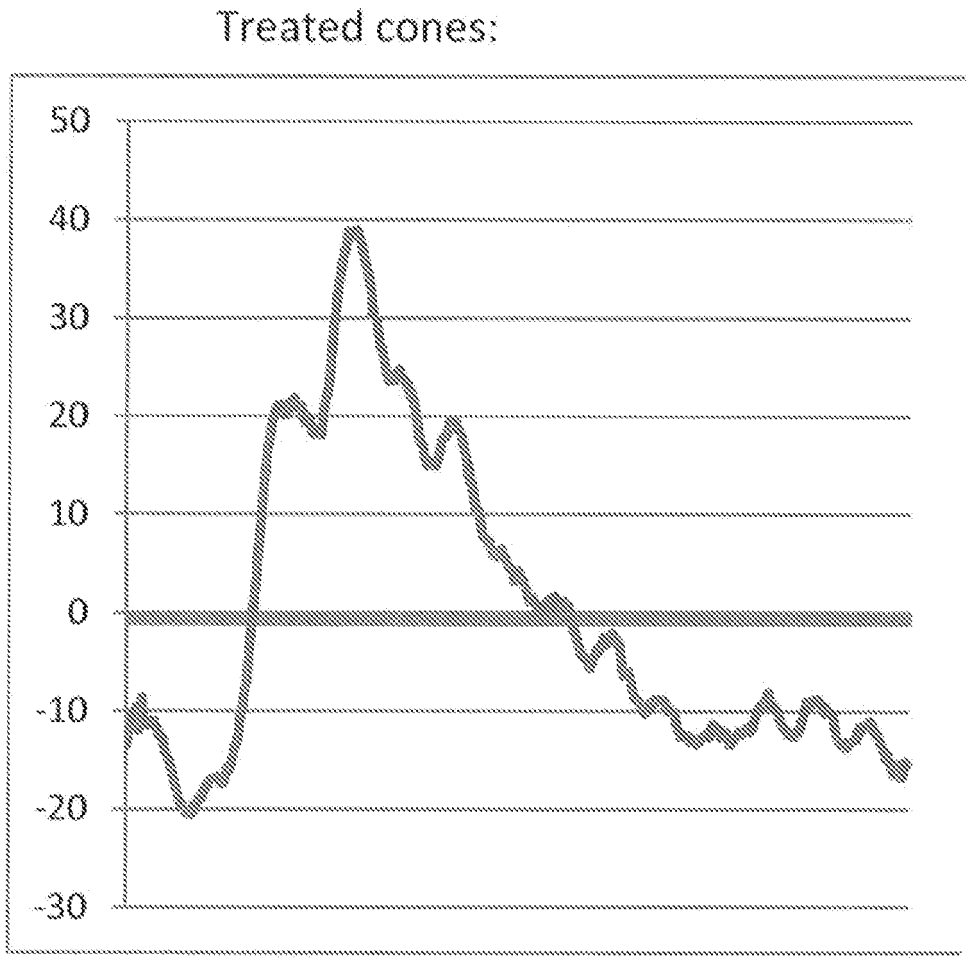


FIG. 19B

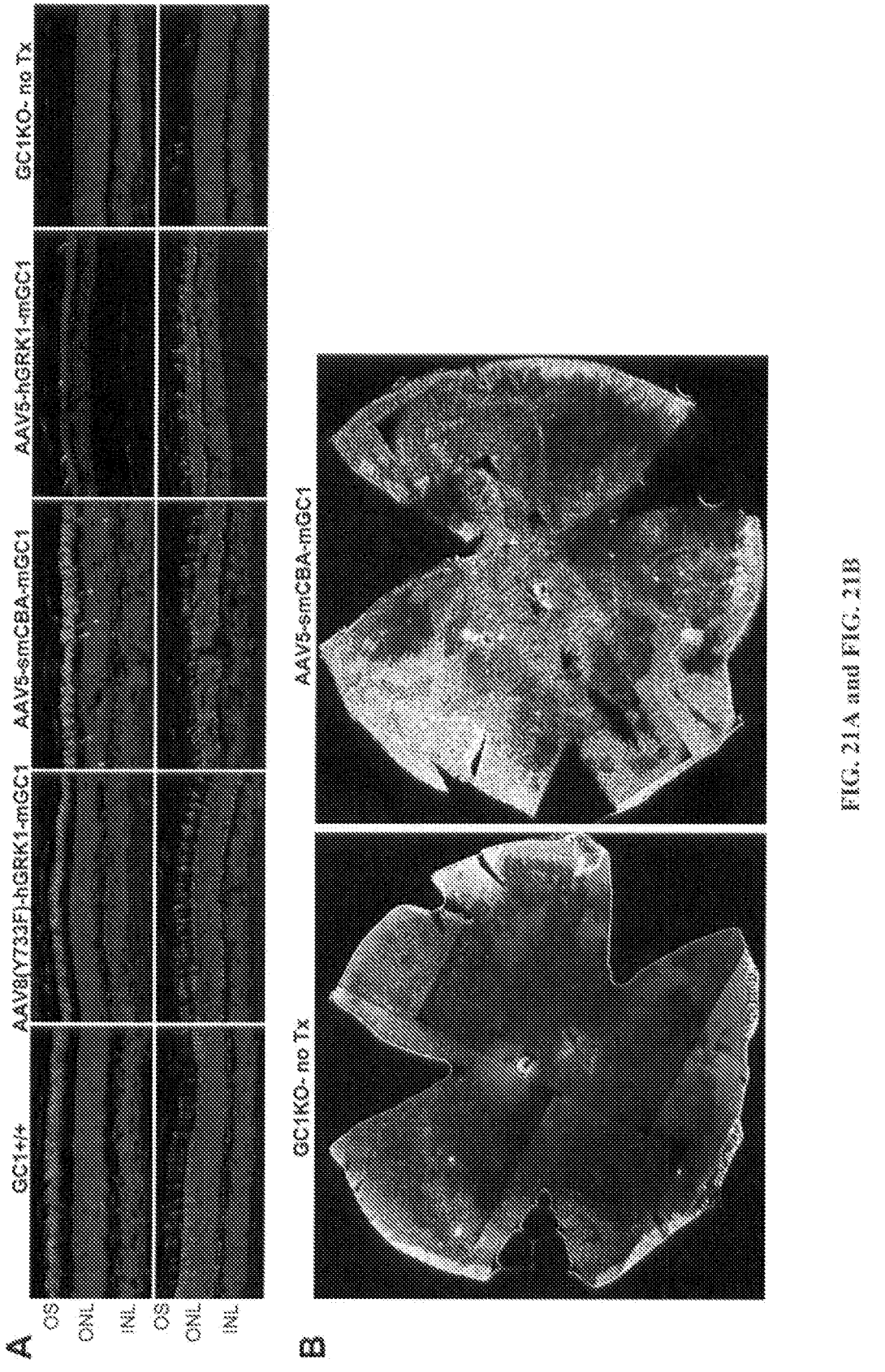


FIG. 21A and FIG. 21B

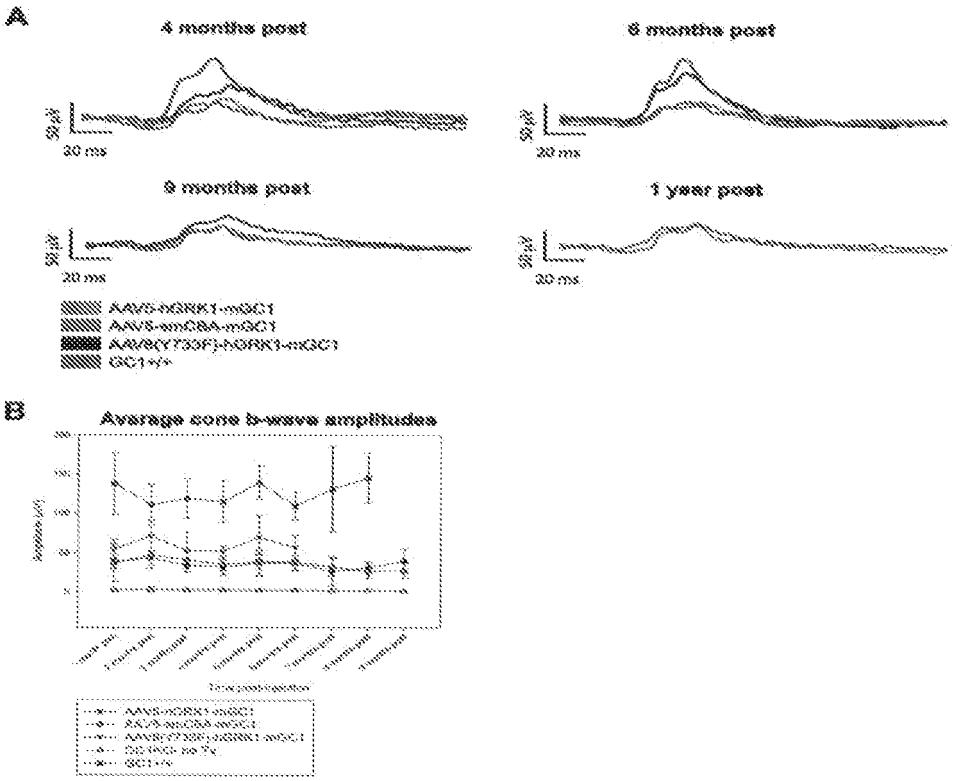


FIG. 22A and FIG. 22B

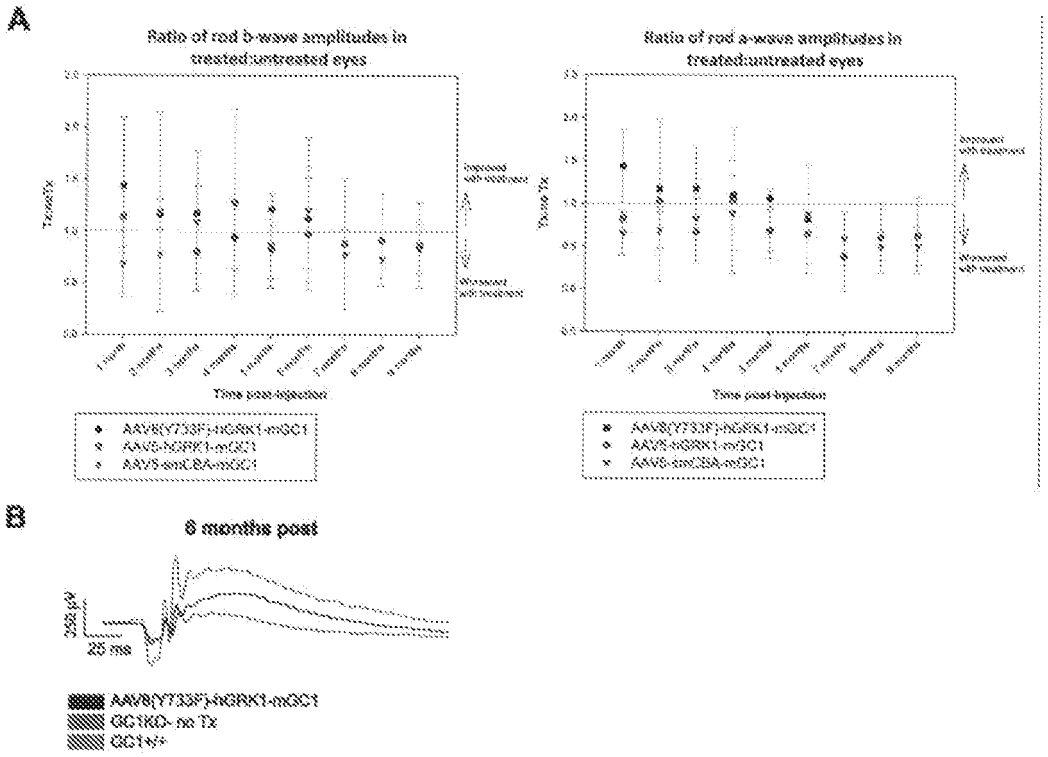


FIG. 23A and FIG. 23B

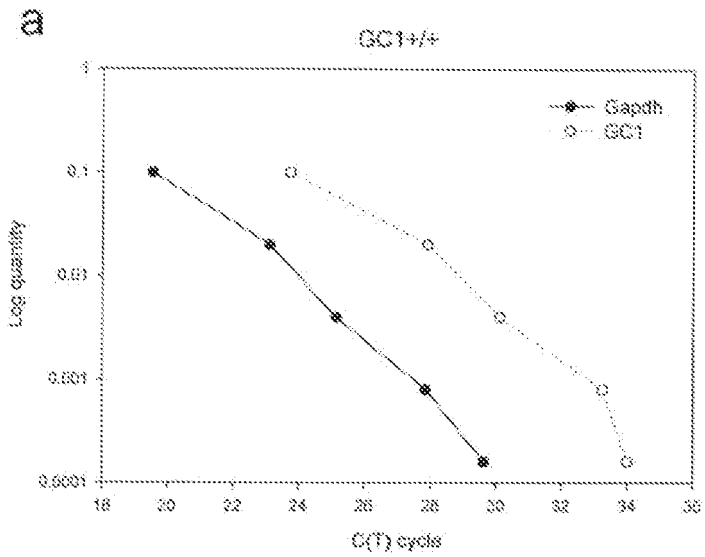


FIG. 24A

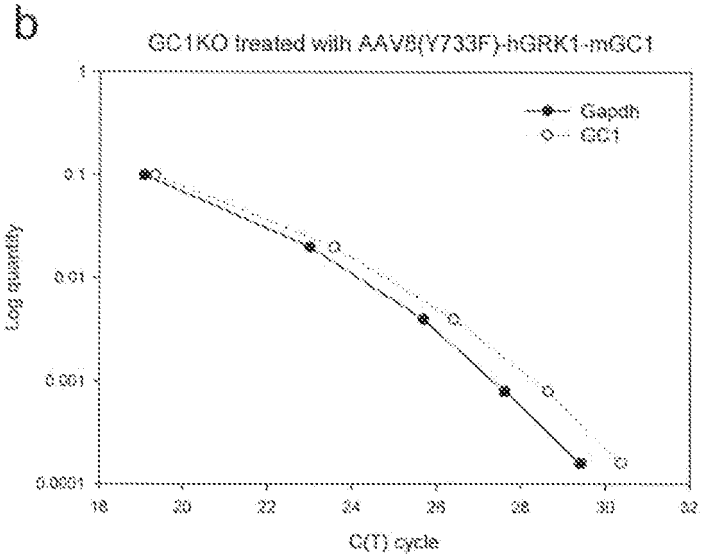


FIG. 24B