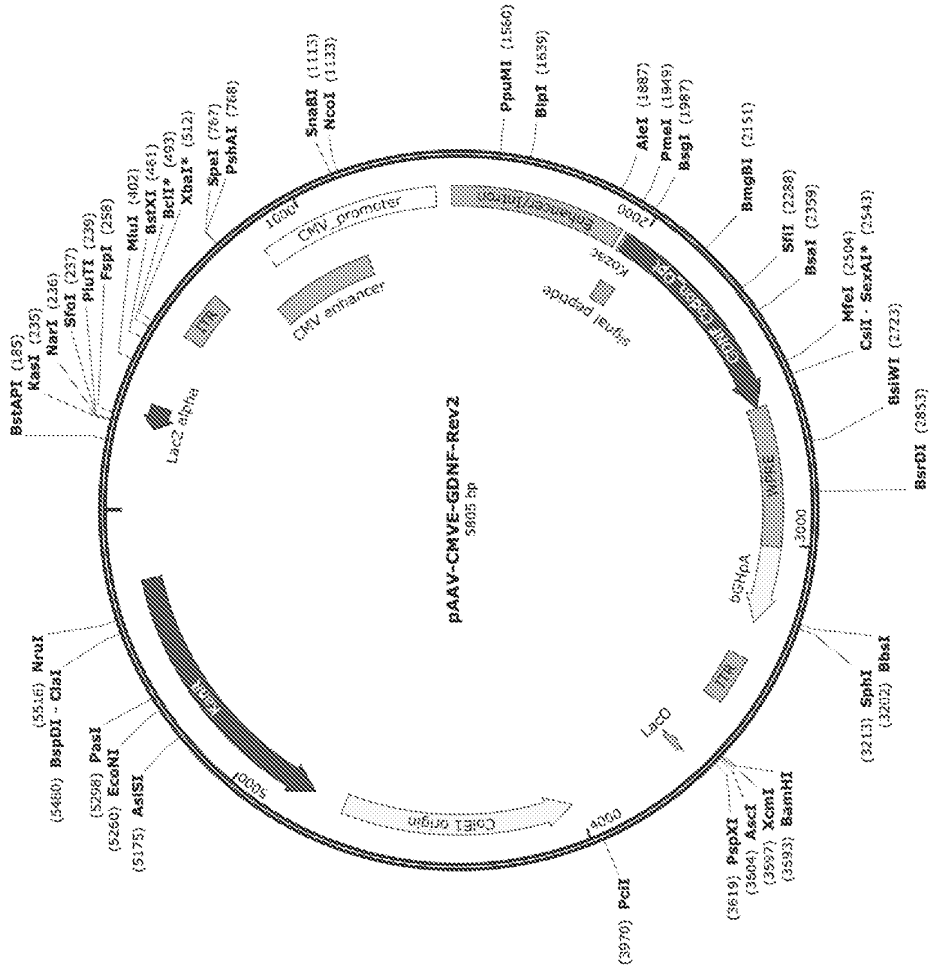

pAAV-CMVE-GDNF-Rev2
5805 bp
1000
2000
3000
4000
5000
CMV promoter
CMV enhancer
Kozak
signal peptide
GDNF mature protein
WPRE
bGHpA
ITR
ITR
LacO
f1 origin
pUC origin
Lac2 alpha
BstAPI (185)
KasI (335)
NarI (336)
SfaI (237)
PluTI (239)
FspI (258)
MluI (402)
BstXI (461)
BclI* (493)
XhaI* (512)
SpeI (767)
PshAI (768)
SnaBI (1113)
NcoI (1133)
PpuMI (1560)
BlpI (1839)
AfeI (1887)
PmeI (1949)
BsgI (1987)
BmgBI (2151)
SfiI (2288)
BssaI (2359)
MfeI (2504)
CaiI - SexAI* (2543)
BsiWI (2723)
BsrDI (3853)
SphI (3213)
BbsI (3282)
PcsI (3970)
PspXI (3619)
AscI (3604)
XcmI (3597)
BamHI (3593)
AsiSI (5175)
EcoNI (5260)
PasI (5258)
BspDI - ClaI (5480)
NruI (5516)

FIG. 1A

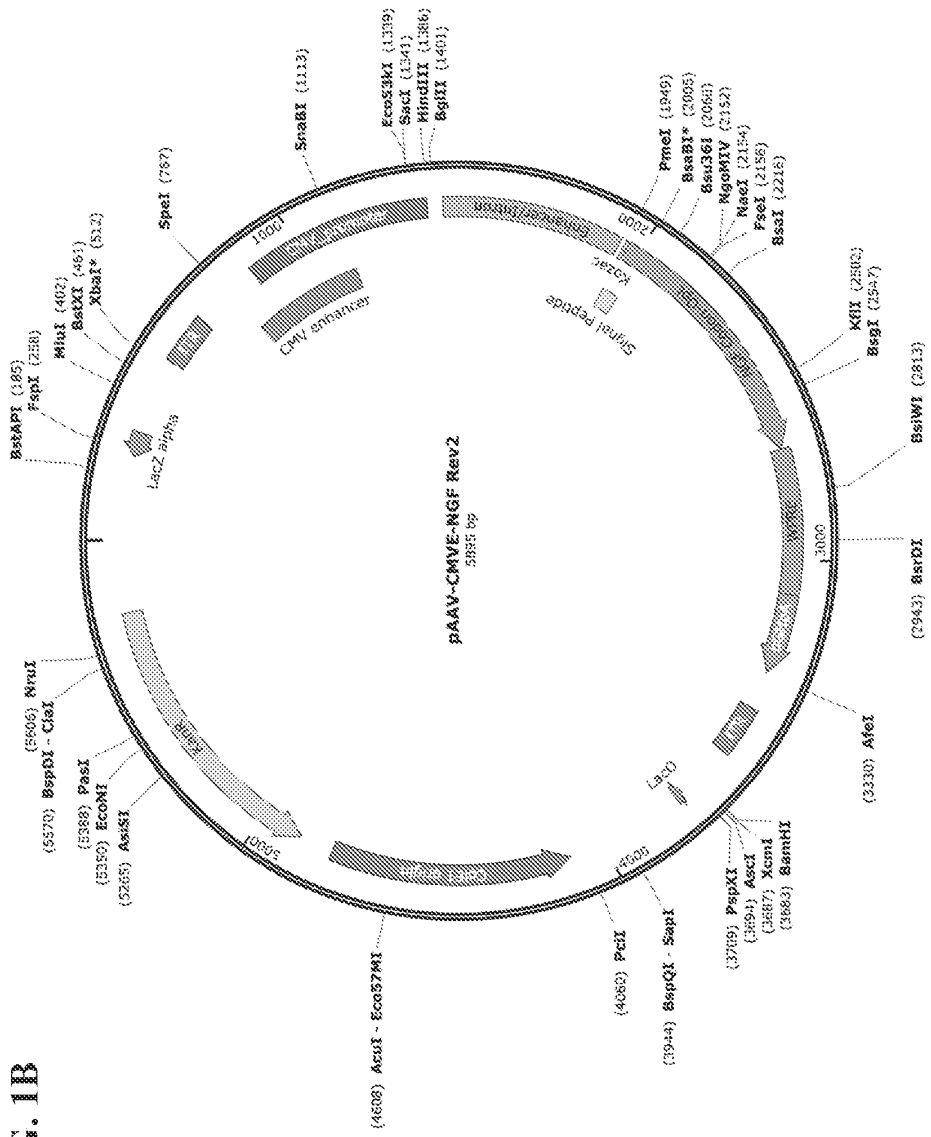

pAAV-CMVE-NGF Rev2
5835 bp
SnaBI (1113)
EcoS9I (1339)
SacI (1341)
HindIII (1386)
BglII (1401)
PmeI (1949)
BsaBI* (2005)
Bsu36I (2068)
MscI (2152)
NaeI (2154)
PsiI (2156)
SsiI (2216)
KfiI (2582)
BsgI (2647)
BsiWI (2813)
BsrDI (2943)
AfeI (3330)
XcmI (3683)
BamHI (3687)
AscI (3691)
PspXI (3709)
SapI (3944)
BspQI (3944)
PciI (4086)
AscI - Eco57MI (4608)
PasI (5368)
EcoNI (5369)
AsiSI (5265)
BspDI - ClaI (5606)
NruI (5670)
SpeI (767)
XbaI* (512)
BstXI (461)
MluI (402)
FspI (258)
BstAPI (185)
LacZ alpha
CMV enhancer
Signal peptide
hNGF
WPRE
bGH poly(A)
ITR
ITR
AmpR
LacO
ori
1000
2000
3000
4000
5000

FIG. 1B

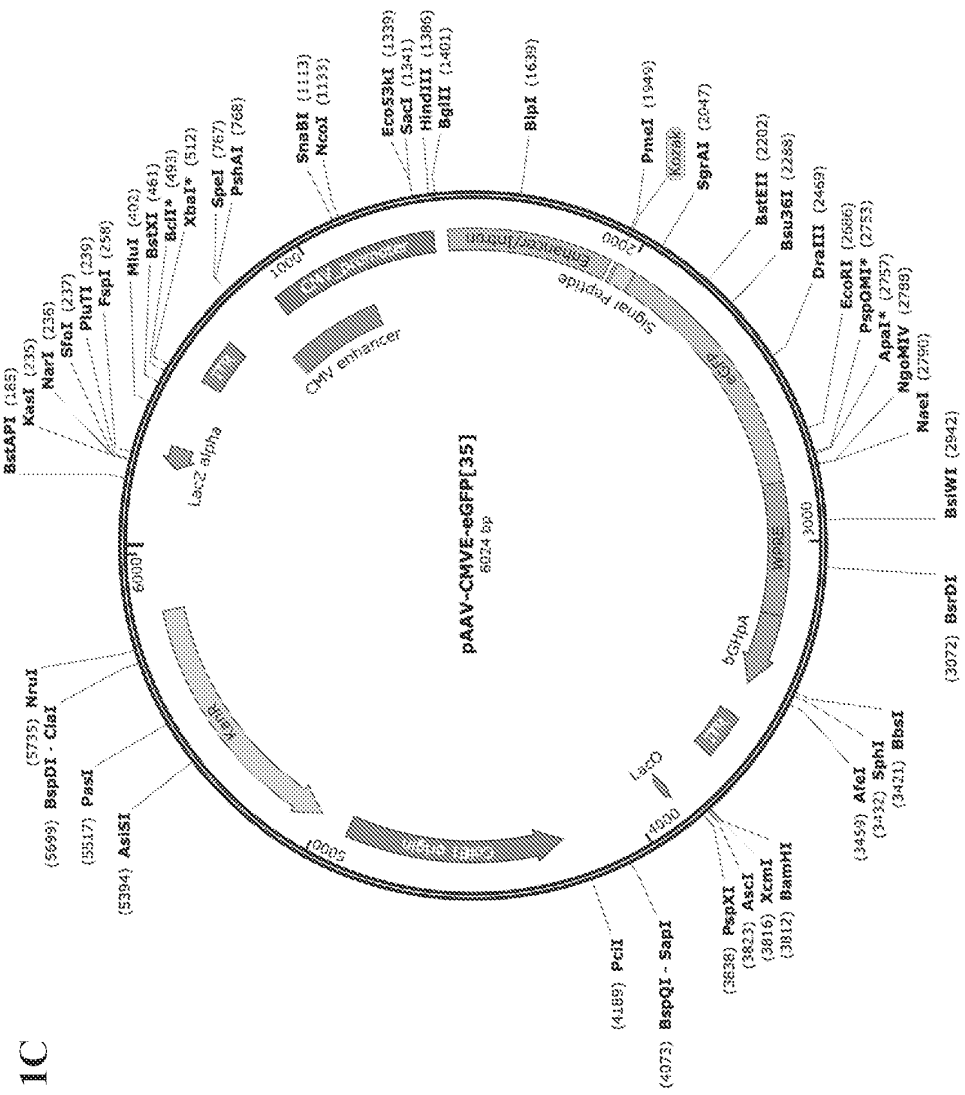

pAAV-CMVE-eGFP[35]
6824 bp
CMV enhancer
Signal Peptide
bGHpA
LacO
Lac2 alpha
1000
2000
3000
4000
5000
6000
BstAPI (185)
KasI (235)
NarI (236)
SfoI (237)
PluTI (239)
FspI (258)
MluI (402)
BstXI (461)
BclI* (493)
XbaI* (512)
SpeI (767)
PshAI (768)
SnaBI (1113)
NcoI (1133)
Eco53kI (1339)
SacI (1341)
HindIII (1386)
BglII (1401)
BlpI (1639)
PmeI (1949)
SgrAI (2047)
BstEII (2202)
Bsu36I (2288)
DraIII (2469)
EcoRI (2686)
PspOMI* (2753)
ApaI* (2757)
NgoMIV (2788)
NaeI (2790)
BsiWI (2942)
(3072) BsrDI
(3459) AfeI
(3482) SphI
(3491) BlnI
(3812) BamHI
(3816) XcmI
(3823) AscI
(3838) PspXI
(4073) BspQI - SapI
(4169) PciI
(5394) AsiSI
(5517) PasI
(5699) BspDI - ClaI
(5735) NruI

FIG. 1C

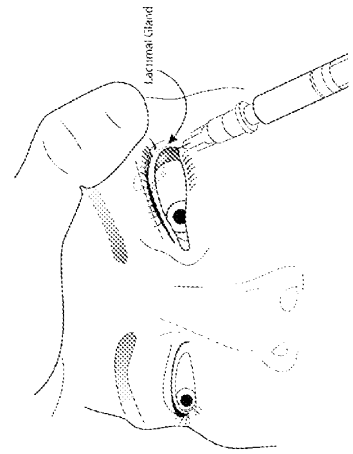


FIG. 2B

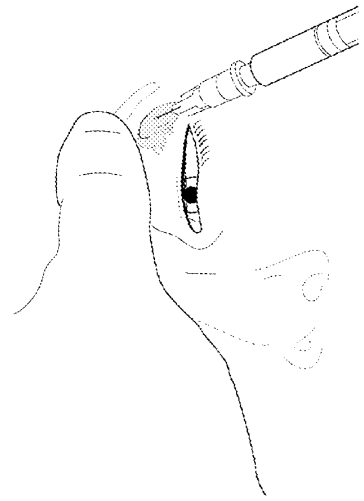


FIG. 2A

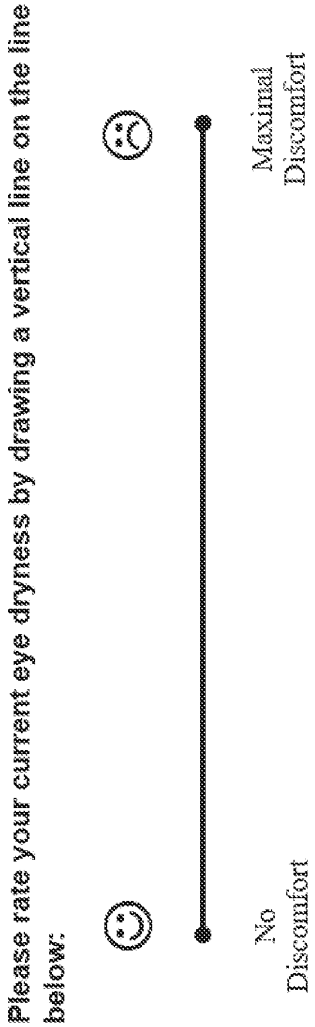

Please rate your current eye dryness by drawing a vertical line on the line below:
No Discomfort
Maximal Discomfort

FIG. 3

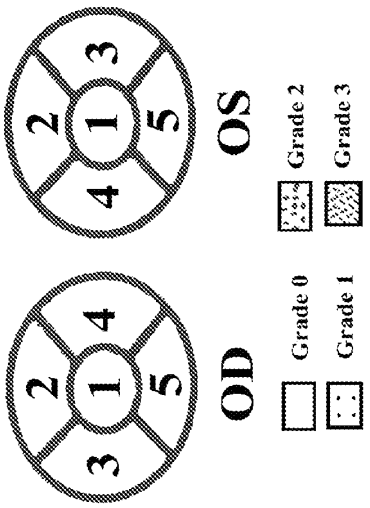


FIG. 4

Mackie's classification of Neurotrophic Keratitis:

Stage I:

- Rose bengal staining of the palpebral conjunctiva Decreased tear breakup time
- Increased viscosity of tear mucus
- Punctate epithelial staining with fluorescein
- Scattered small facets of dried epithelium (Gaule spots)

Stage II:

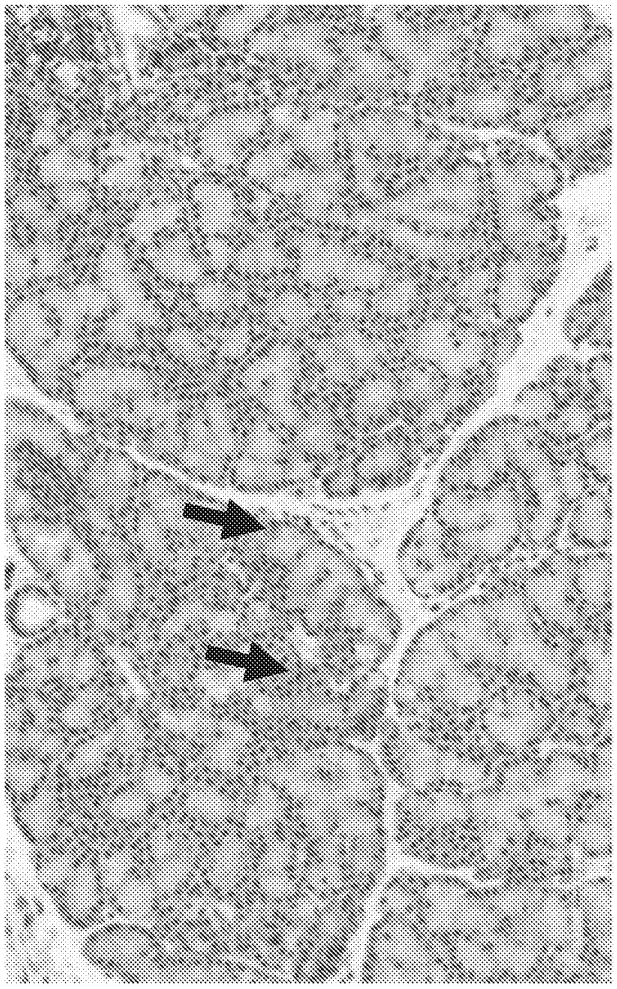
- Acute loss of epithelium, usually under the upper lid Surrounding rim of loose epithelium
- Stromal edema
- Aqueous cells and flare
- Edges of the defect become smooth and rolled with time

Stage III:

Stromal lysis, sometimes resulting in corneal perforation

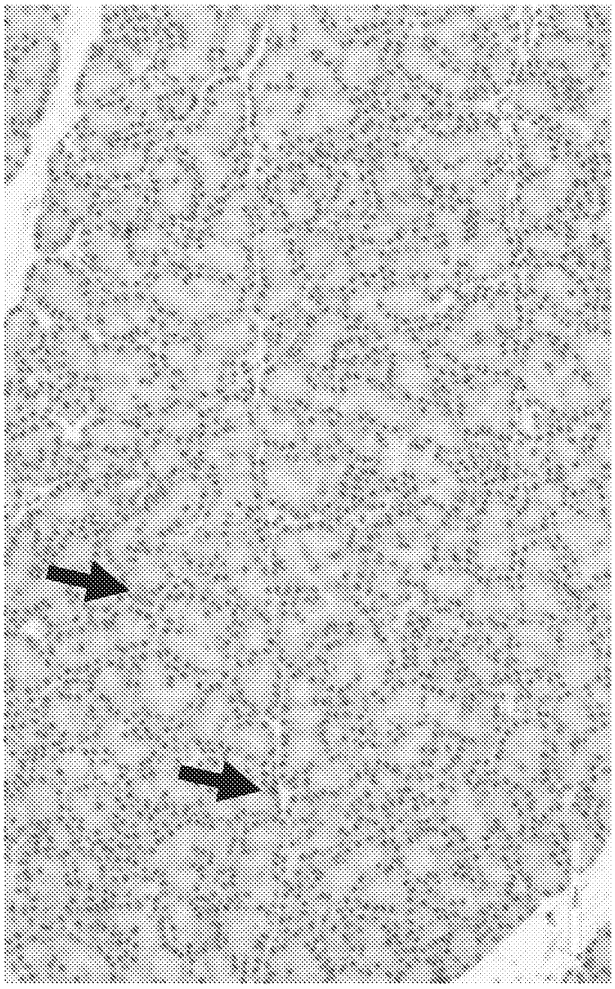
Adapted from: Groos EB. Neurotrophic keratitis. In: Krachmer JH, Mannis MJ, Holland EJ (eds.) Cornea 2nd Ed: Fundamentals, Diagnosis and Management. Mosby: Philadelphia, 2005, p 1191.

FIG. 5



Animal #2002, Right Lacrimal Gland OC-100a 6.2 x 10^{12} GC/mL

FIG. 6A



Animal #3001, Left Lacrimal Gland OC-100b 1 x 10^{12} GC/mL

FIG. 6B

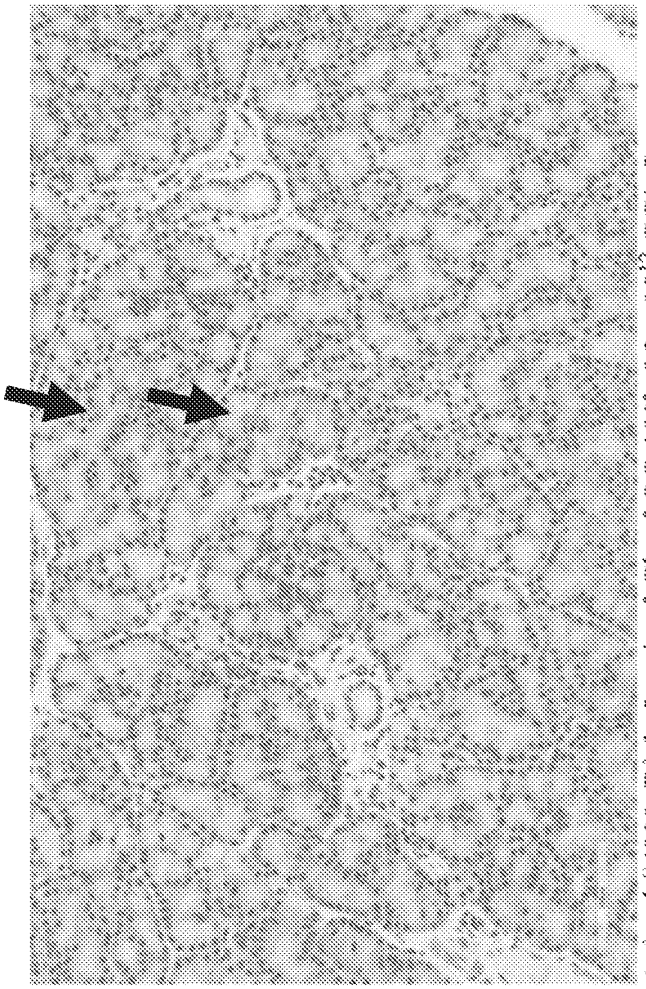


FIG. 6C

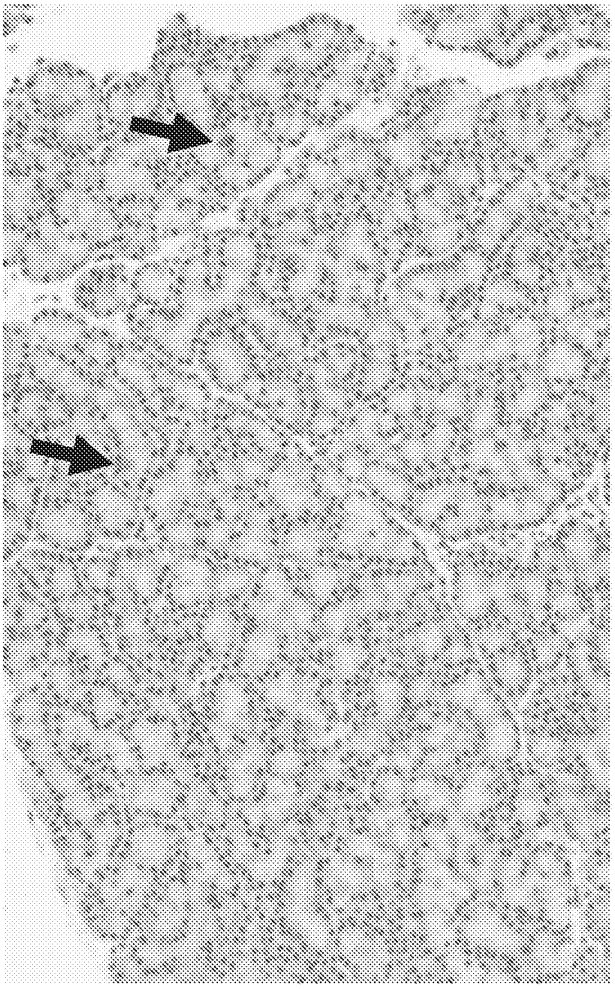


FIG. 6D

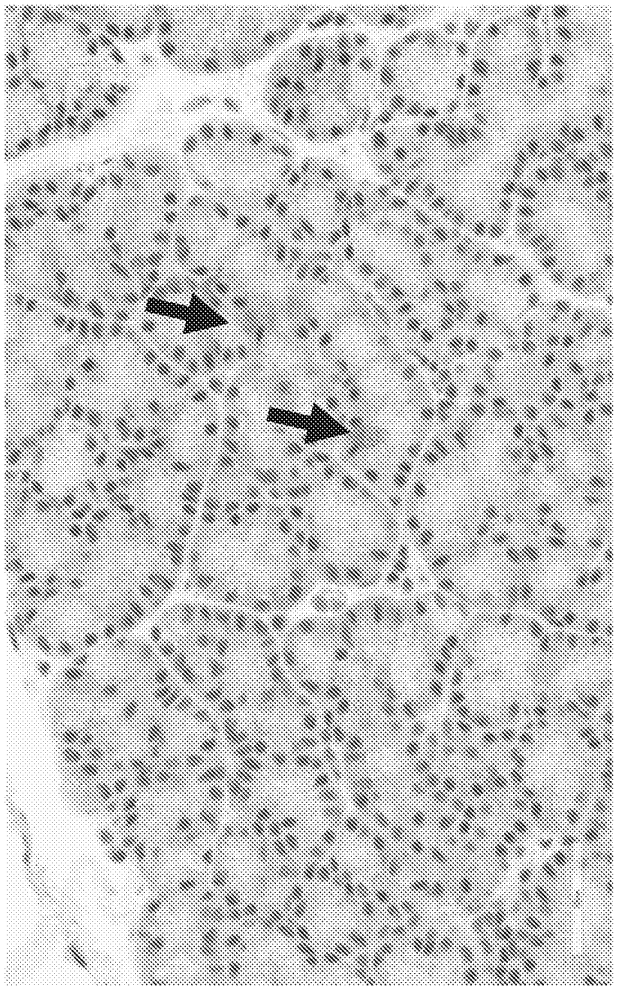


FIG. 6E

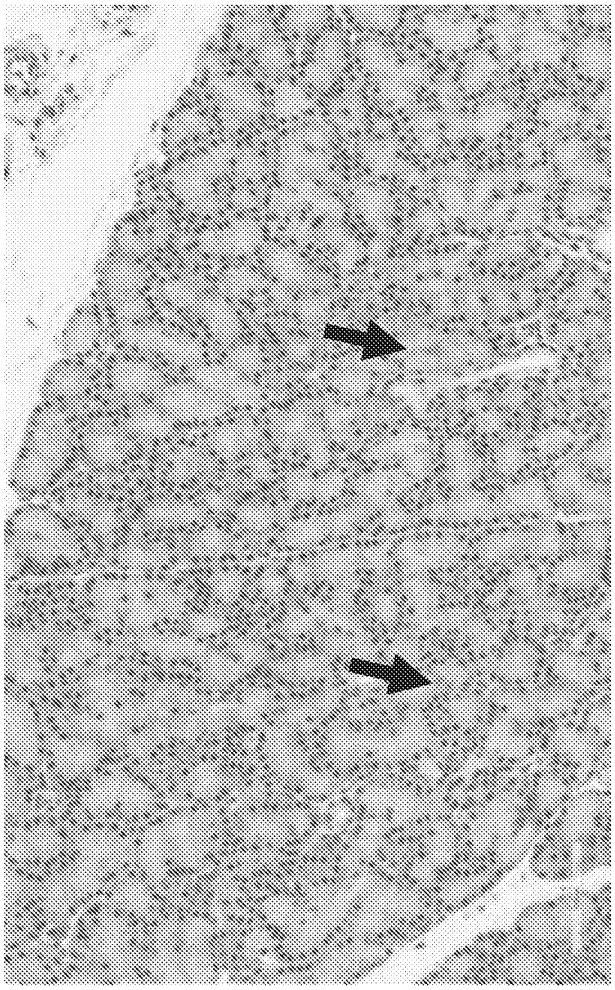
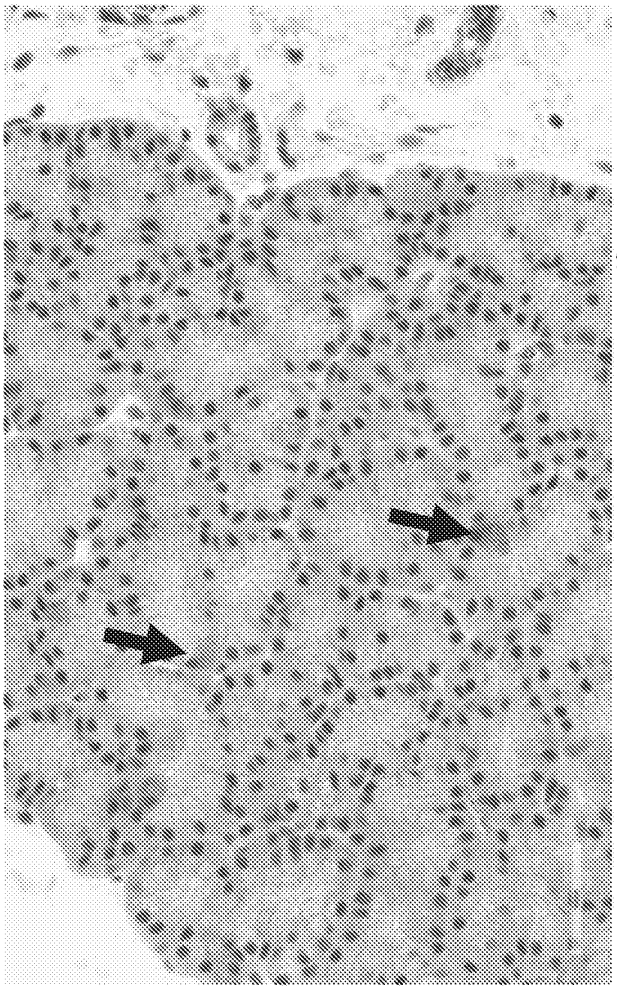


FIG. 6F



Animal #4002. Right Lacrimal Gland OC-100b 6.2 x 10^{12} GC/mL

FIG. 6G

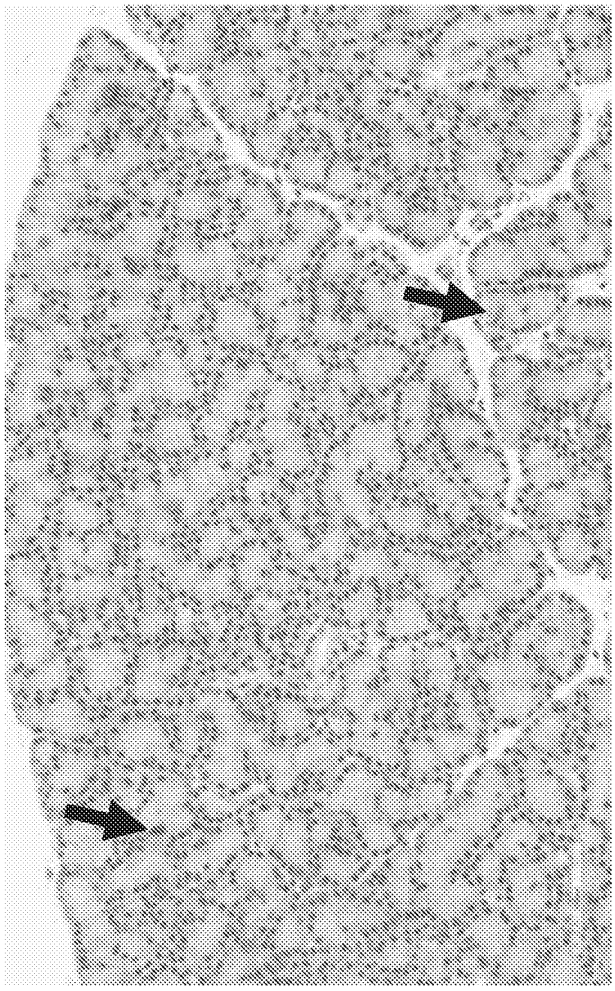


FIG. 6H

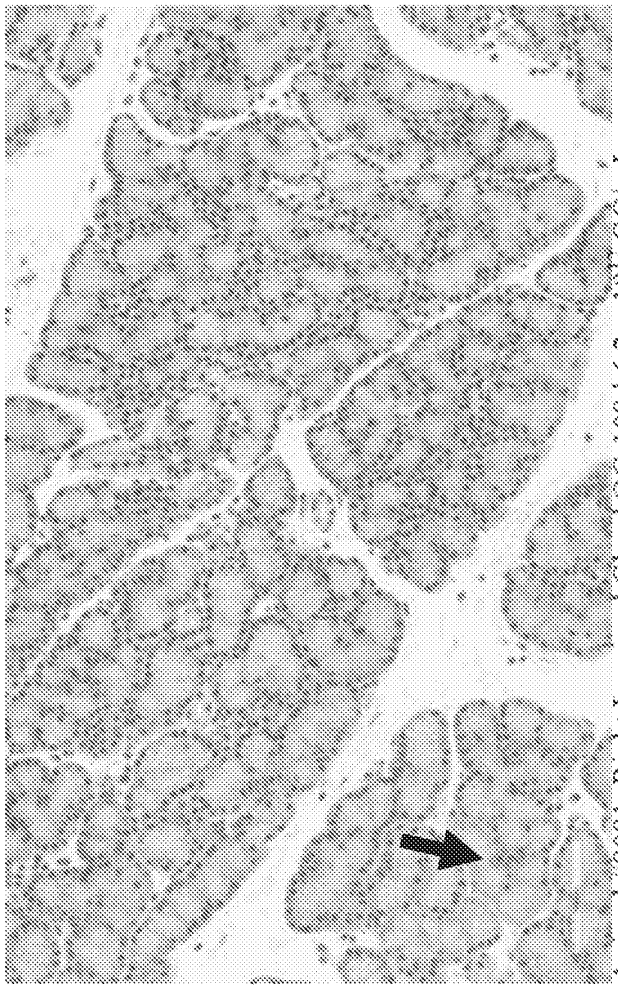
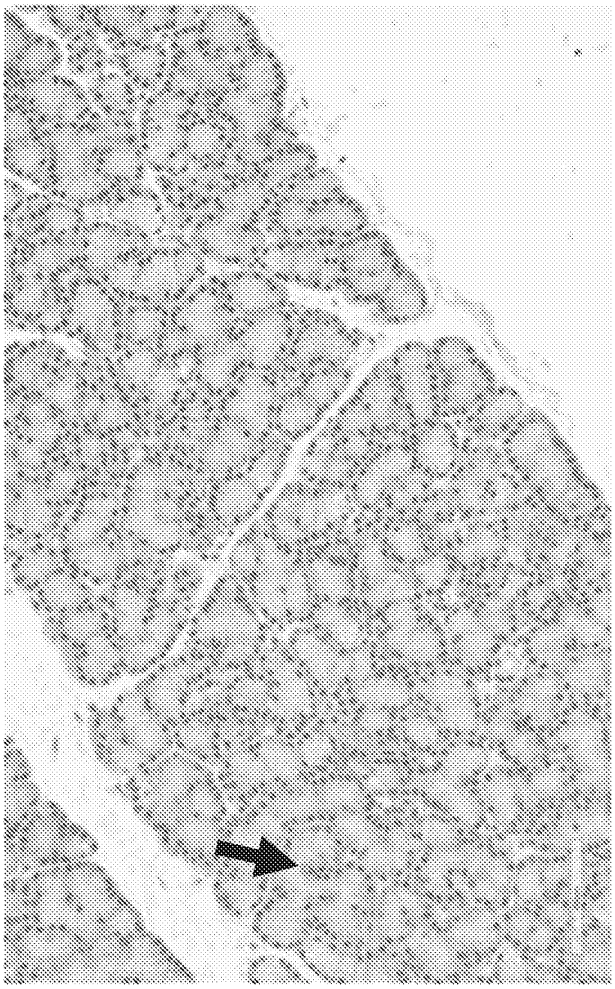


FIG. 6I



Animal #S001. Left Lacrimal Gland OC-100d 6.2×10^{12} GC/mL

FIG. 6J

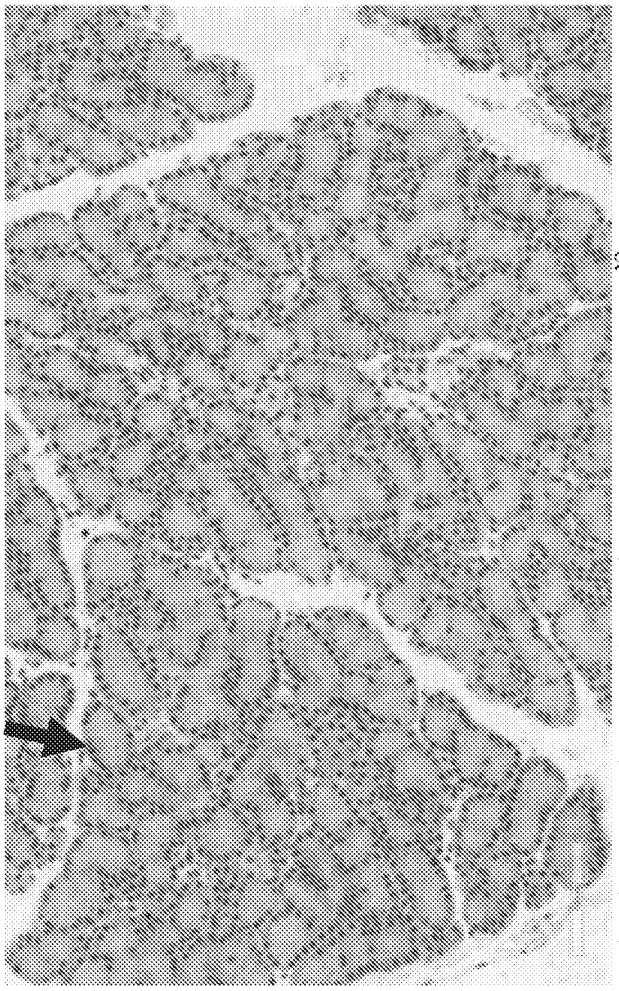


FIG. 6K

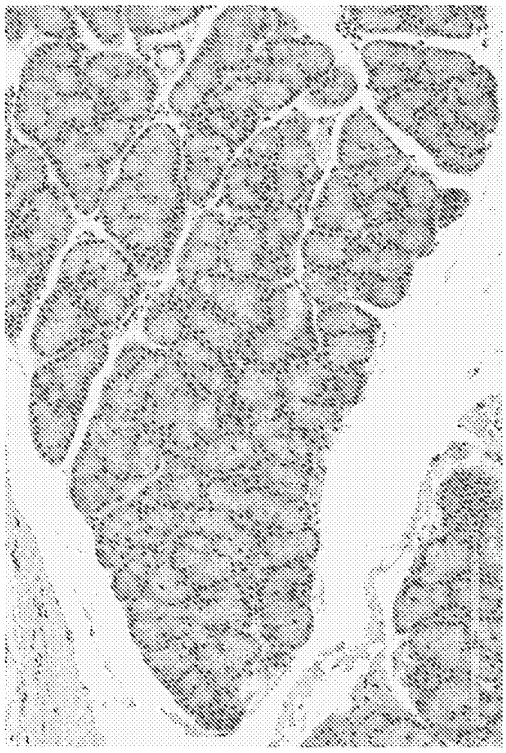


FIG. 7B

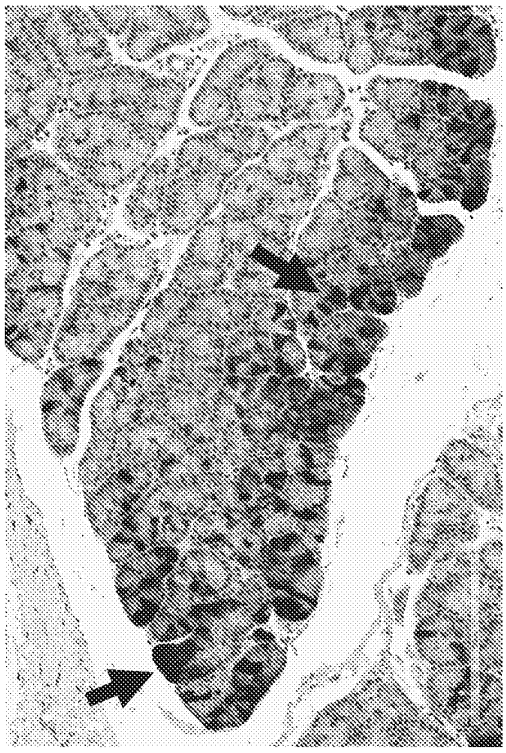


FIG. 7A



FIG. 7C

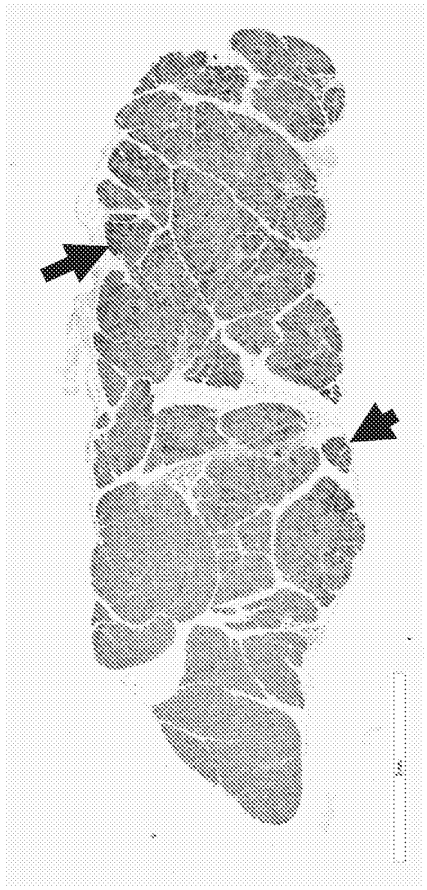


FIG. 7D

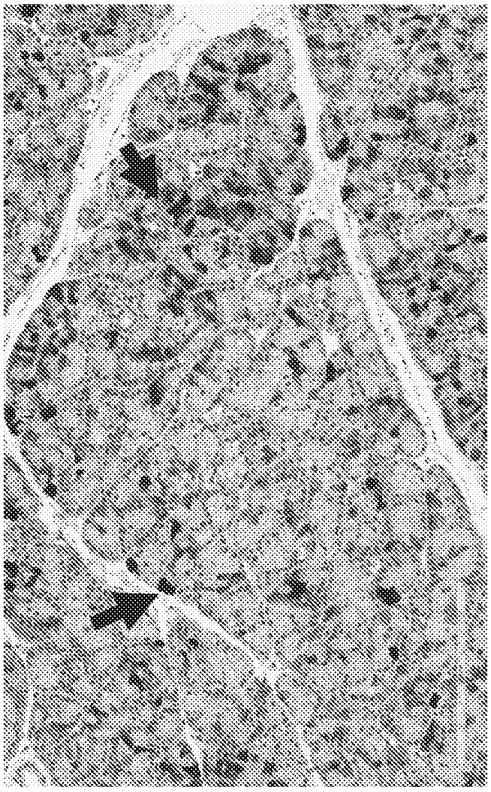


FIG. 7E

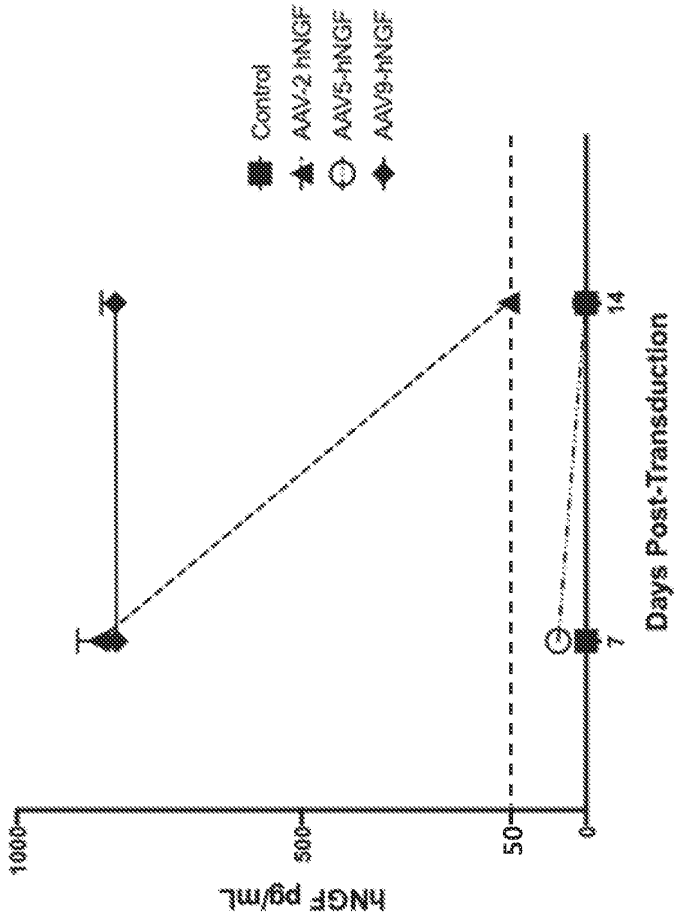

Tear Protein Levels
hNGF pg/mL
1000
500
50
0
Control
AAV-2 hNGF
AAV5-hNGF
AAV9-hNGF
7
14
Days Post-Transduction

FIG. 8

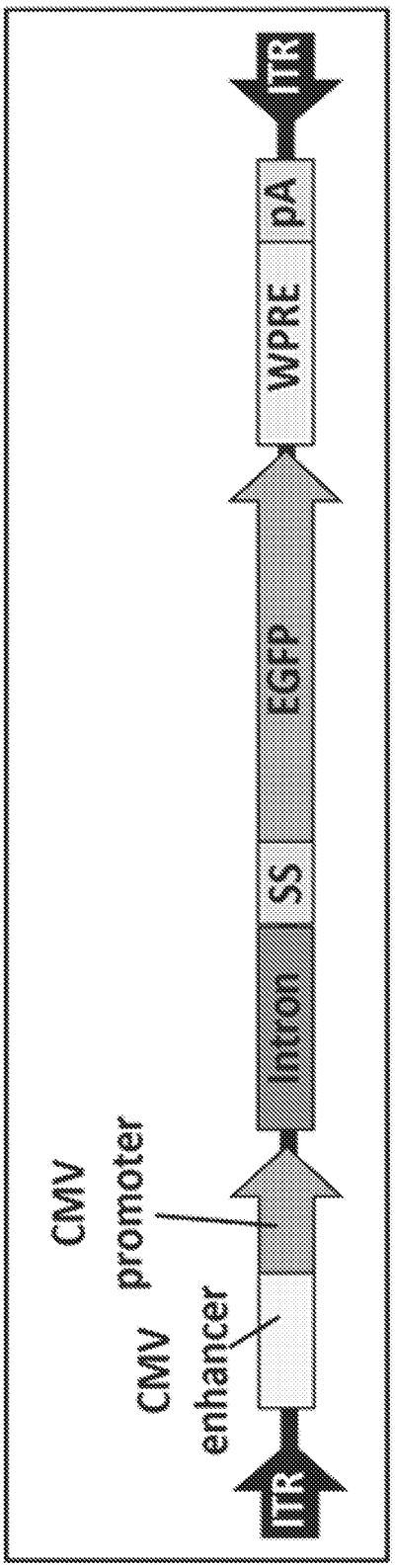


FIG. 9

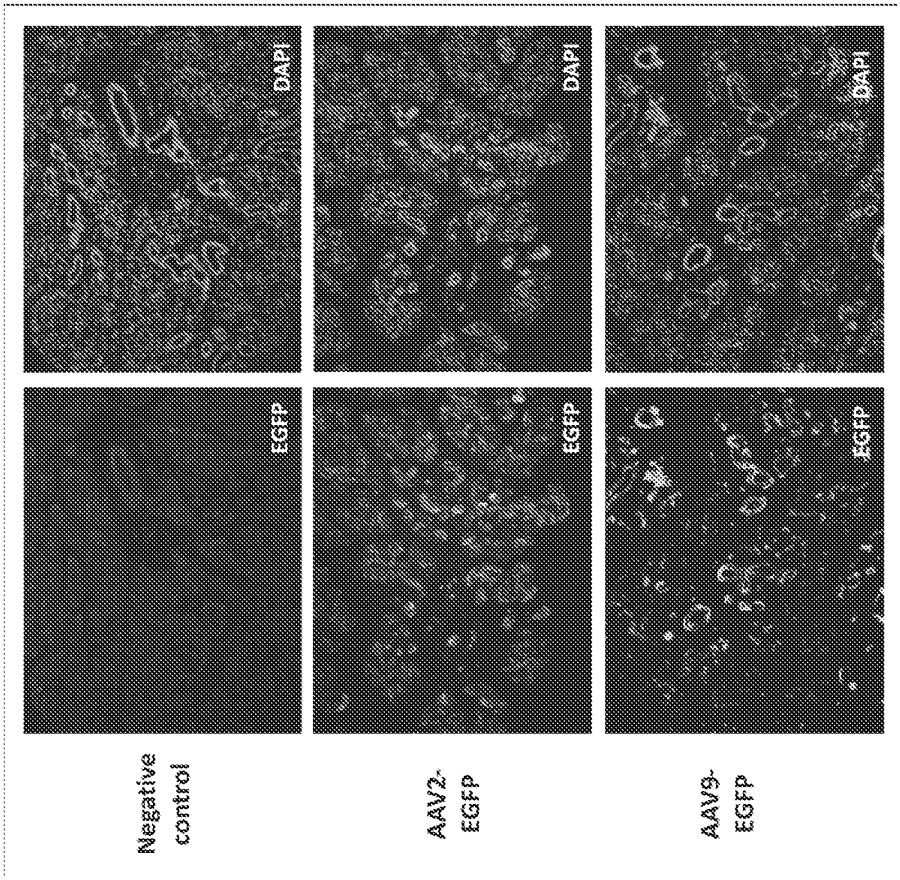


FIG. 10

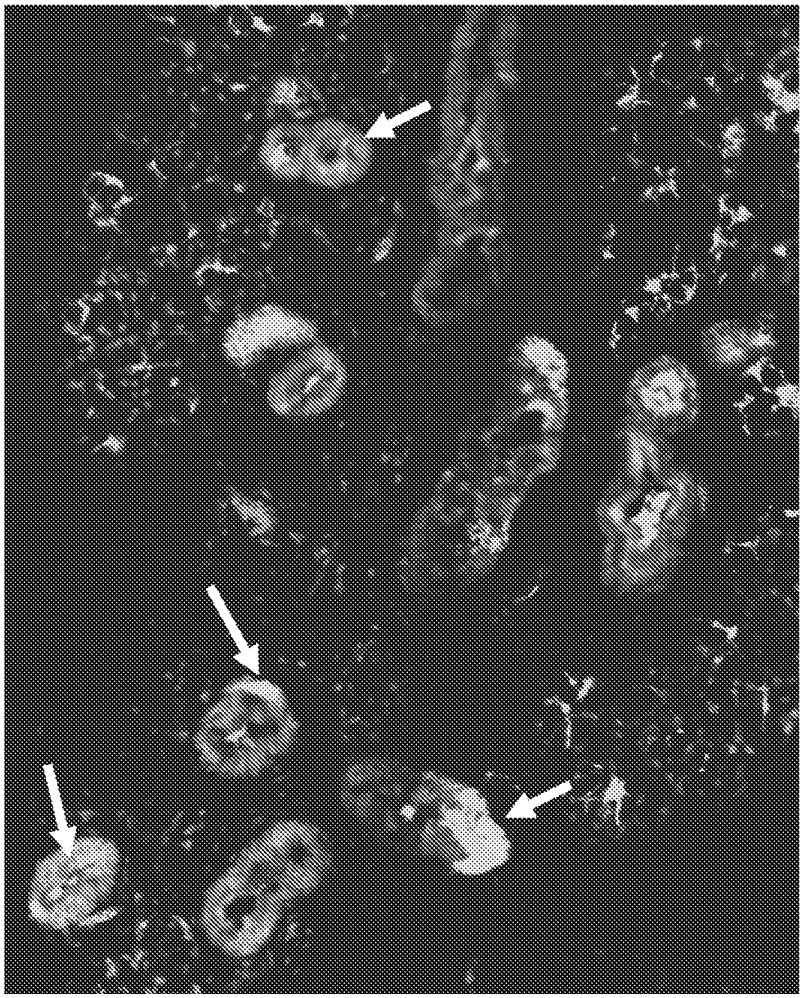


FIG. 11

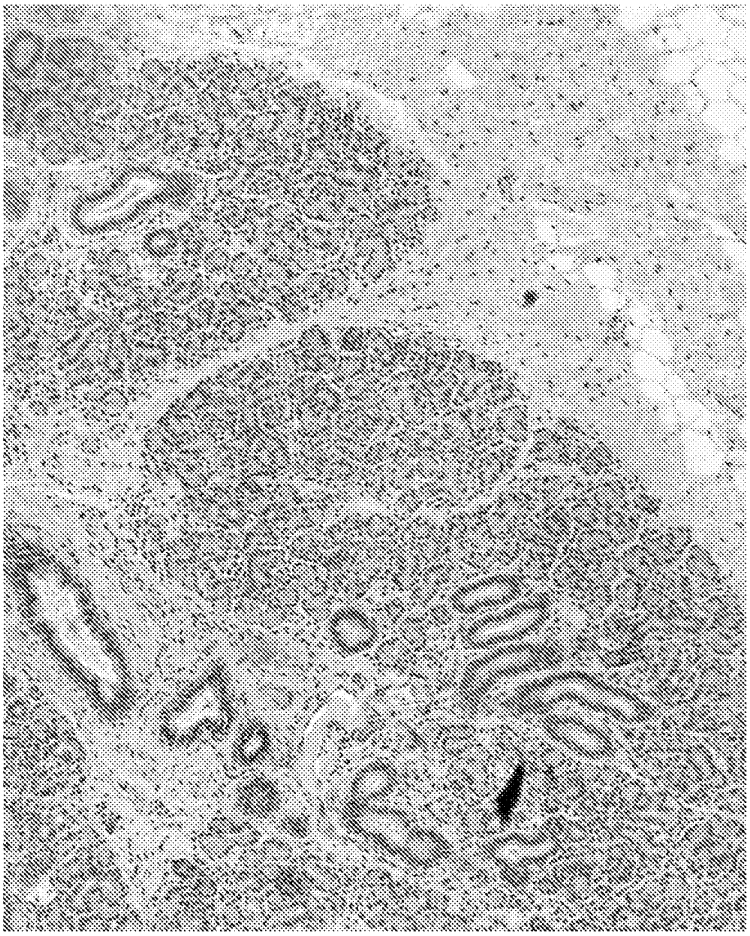


FIG. 12

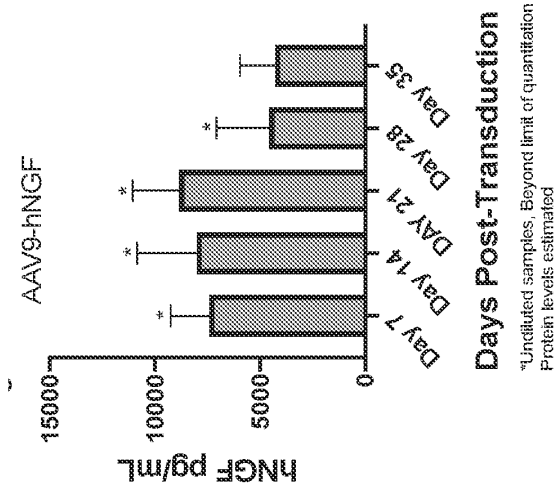


FIG. 13C

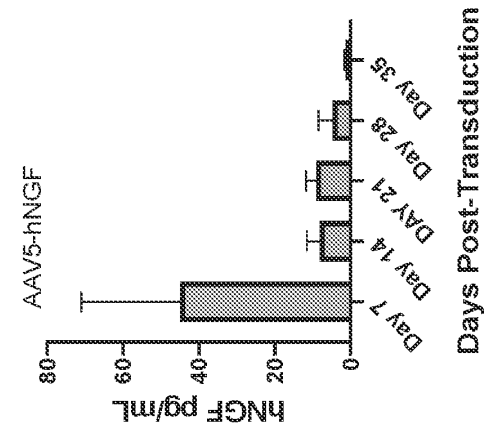


FIG. 13B

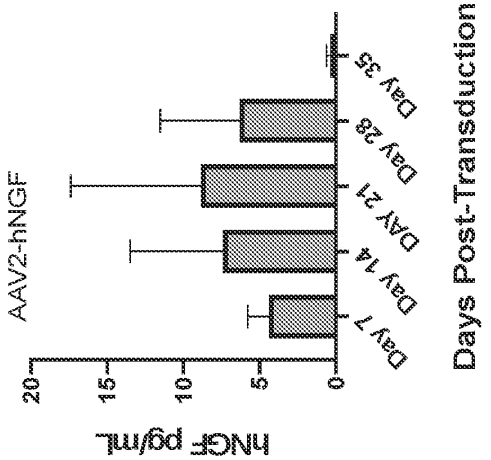


FIG. 13A

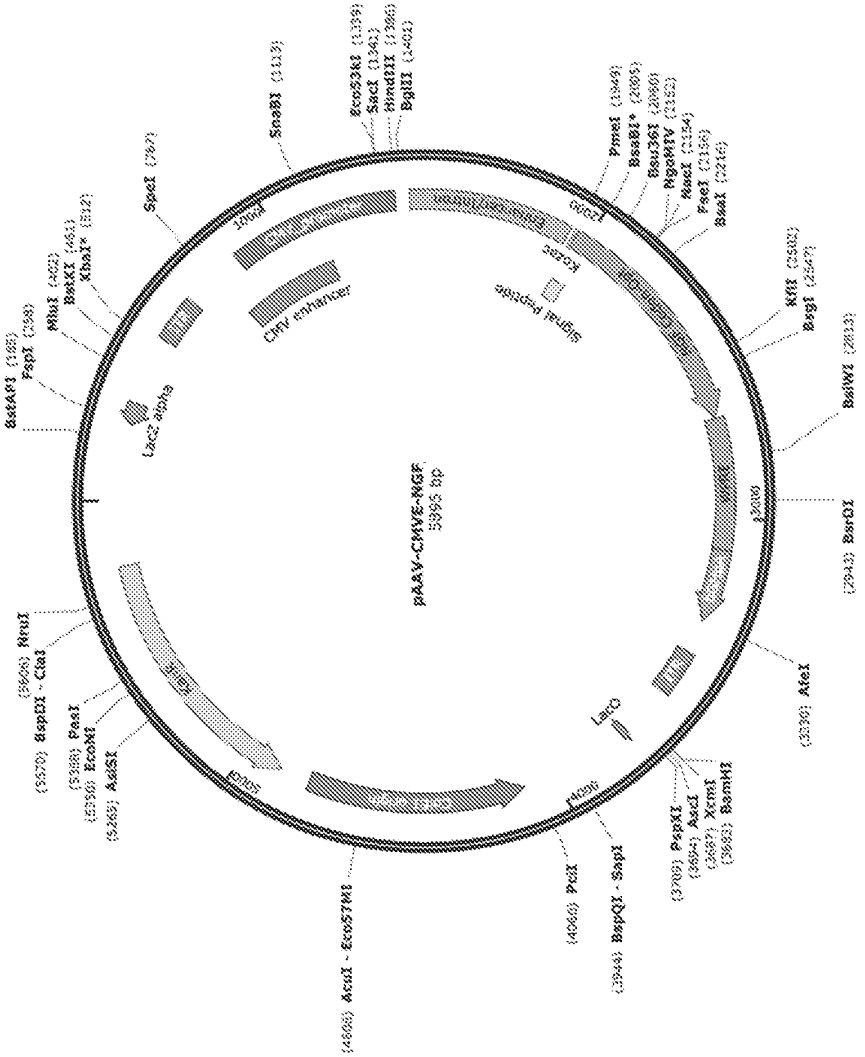

pAAV-CMVE-NGF
5995 bp
CMV enhancer
Signal Peptide
lacZ alpha
ITR
ITR
SpeI (767)
SnaBI (1113)
Eco53kI (1399)
SacI (1342)
HindIII (1396)
BglII (1402)
PmeI (1949)
BsaBI* (2069)
Bsu36I (2096)
PgaHIV (2152)
NaeI (2154)
FseI (2156)
BssHI (2216)
KflI (2502)
BsgI (2547)
BstWI (2813)
BsrDI (2943)
AflII (3396)
AscI (3694)
XcmI (3697)
BamHI (3863)
PspXI (3709)
PciI (4096)
BspQI - SapI (3944)
AccI - Eco57MI (4686)
BspDI - ClaI (5670)
PasI (5988)
EcoNI (6756)
AatII (5268)
NruI (5626)
BstAPI (168)
PspI (258)
MluI (402)
BsrBI (461)
KbaI* (512)

FIG. 14