Fig. 1

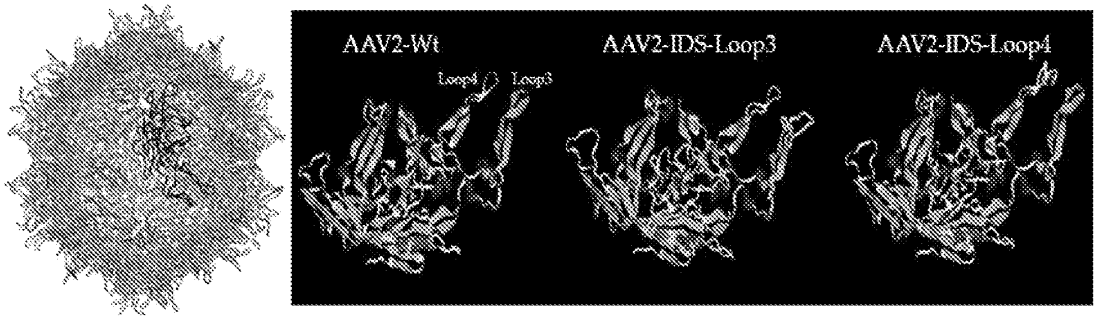


Fig. 2

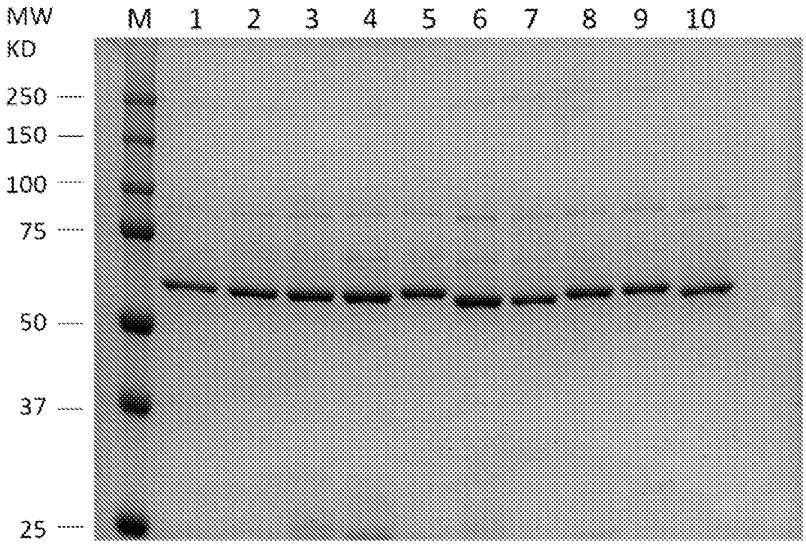


Fig. 3A

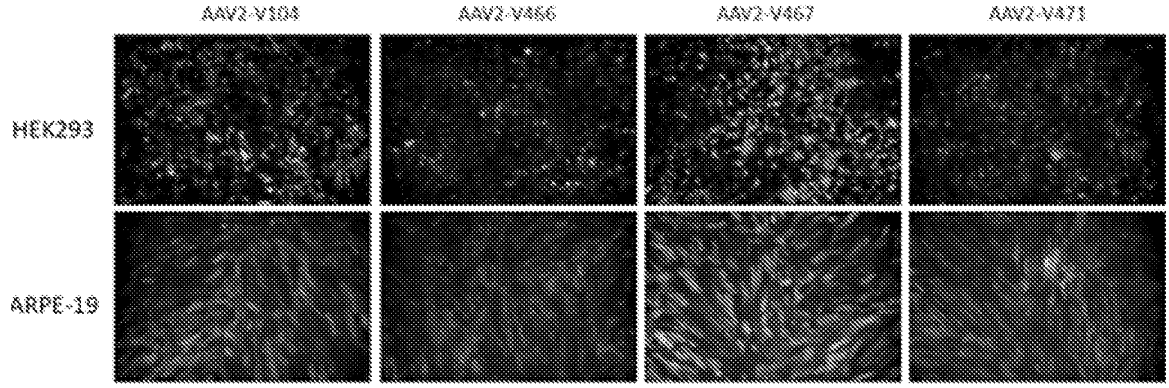

AAV2-V104
AAV2-V466
AAV2-V467
AAV2-V471
HEK293
ARPE-19

Fig. 3B

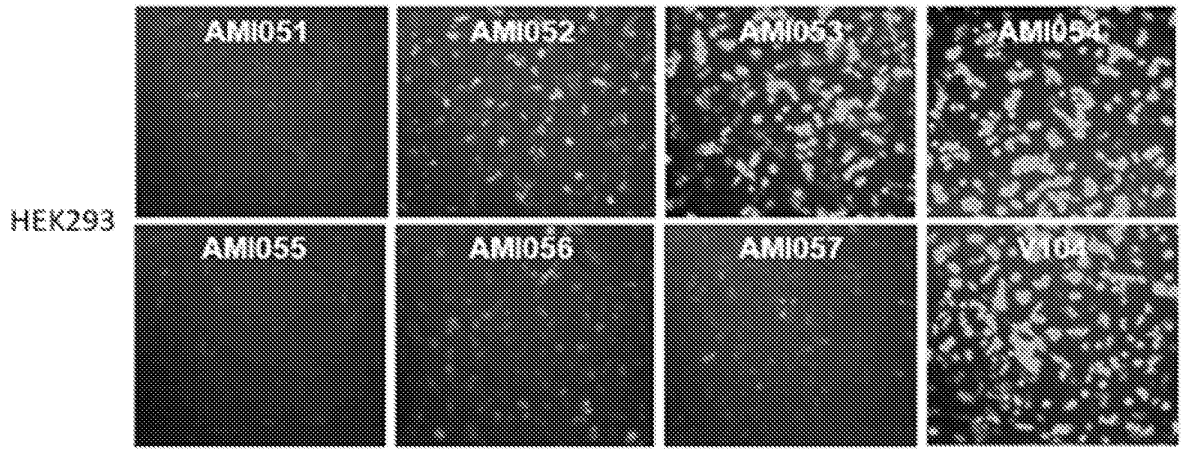
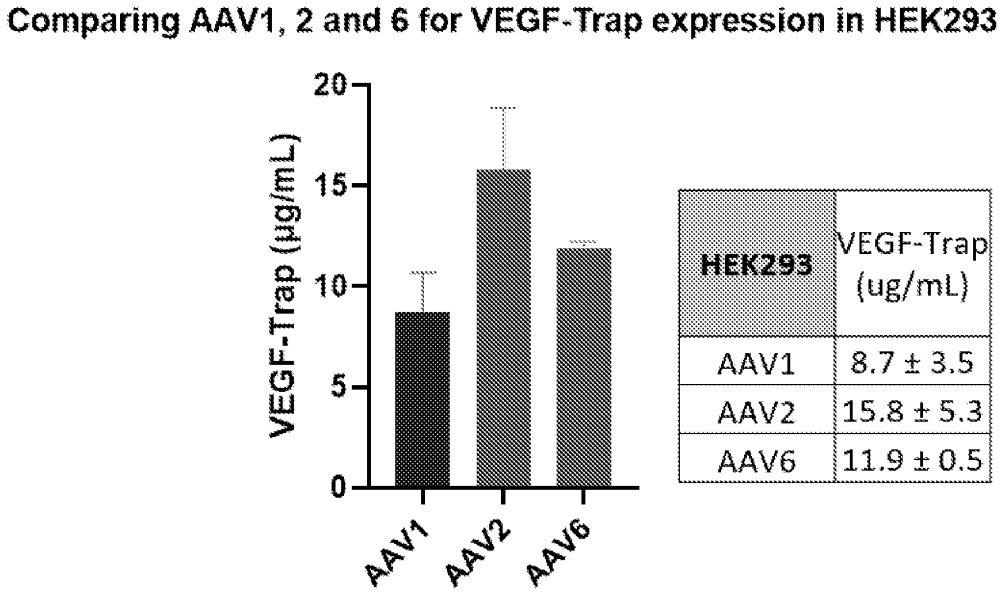
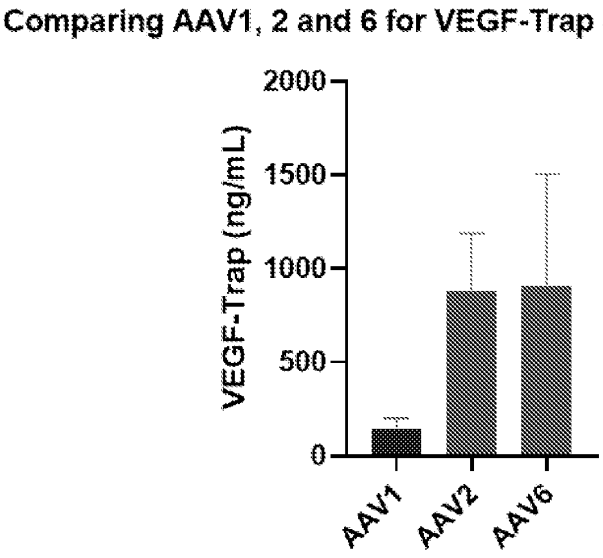

AMI051
AMI052
AMI053
AMI054
HEK293
AMI055
AMI056
AMI057
V104

Fig. 3C



HEK293	VEGF-Trap (ug/mL)
AAV1	8.7 ± 3.5
AAV2	15.8 ± 5.3
AAV6	11.9 ± 0.5

Fig. 3D



ARPE-19	VEGF-Trap (ng/mL)
AAV1	142.1 ± 82.3
AAV2	881 ± 434.7
AAV6	908.4 ± 842.1

Fig. 4

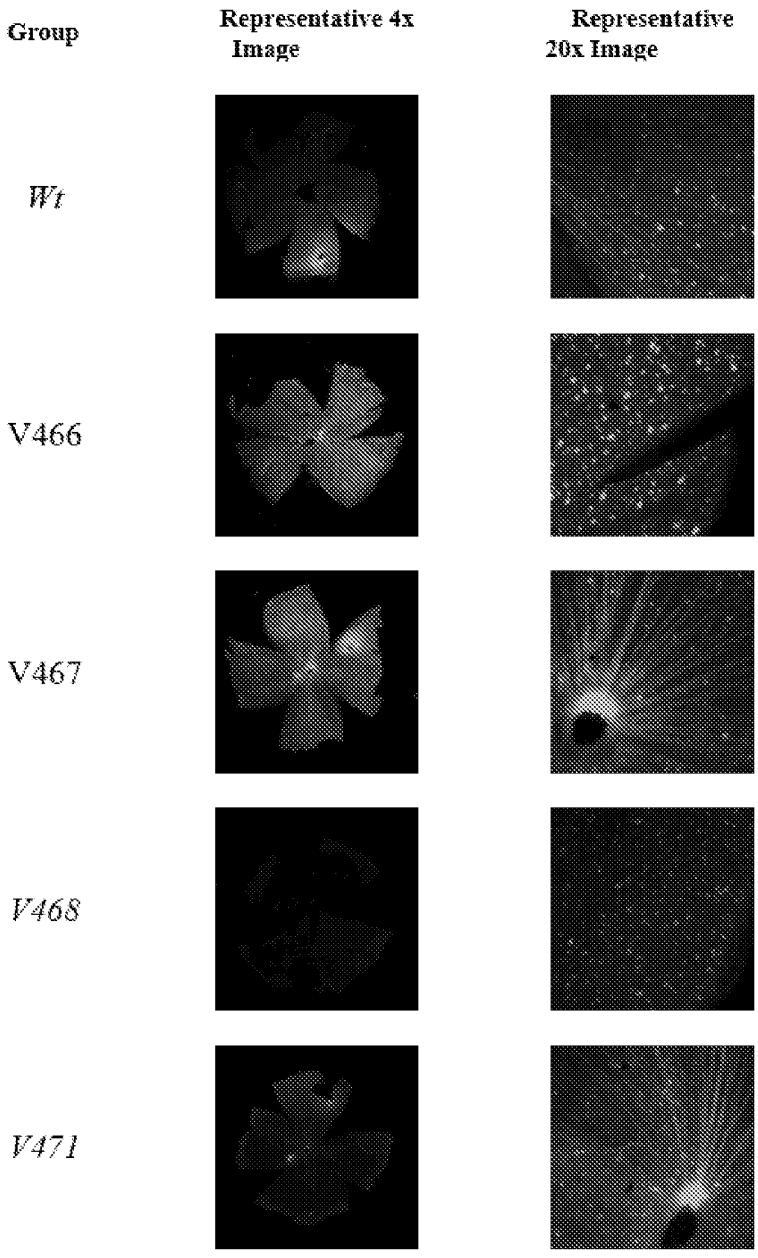

Group
Representative 4x Image
Representative 20x Image
Wt
V466
V467
V468
V471

Fig. 5

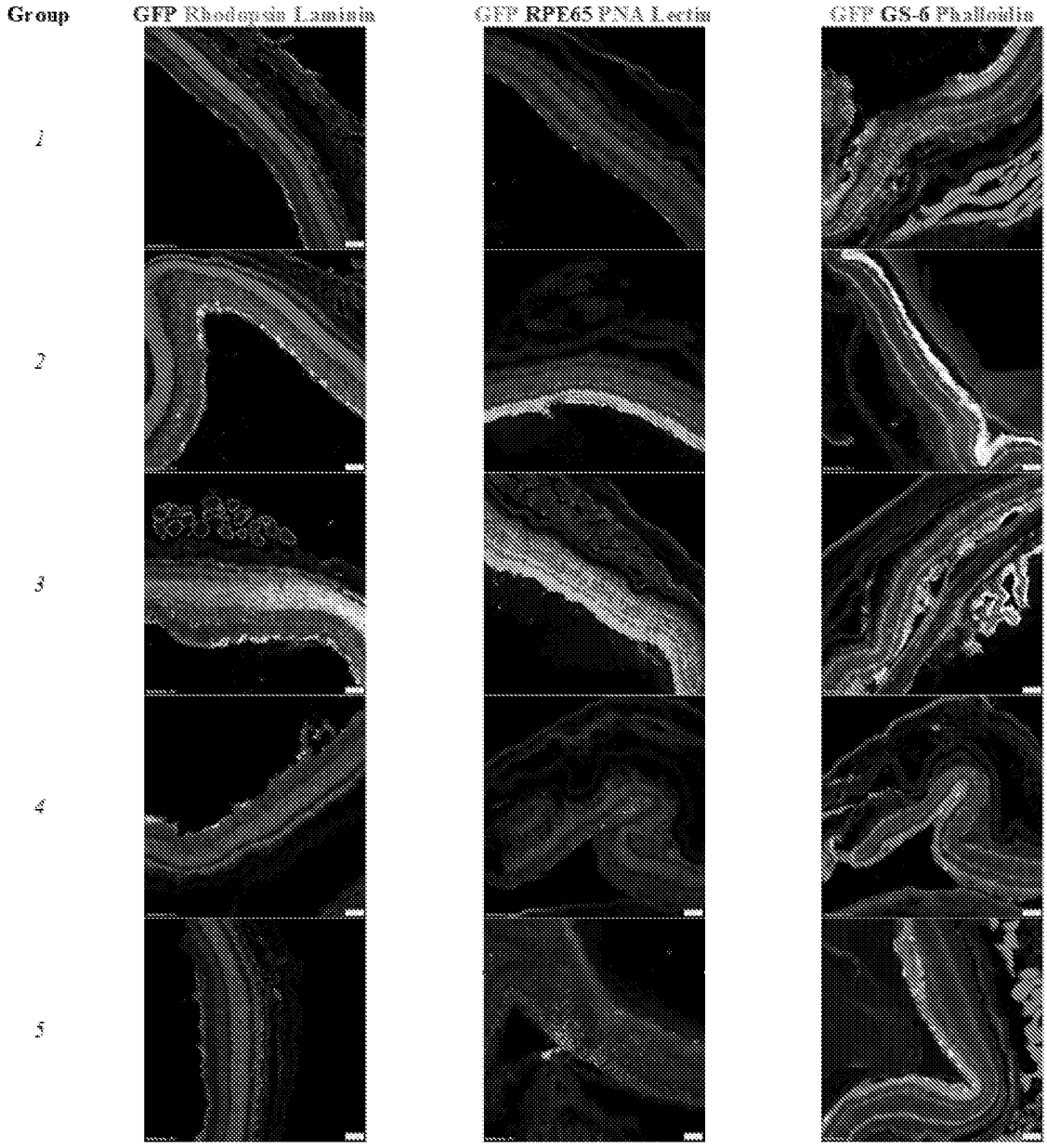

Group
GFP Rhodopsin Laminin
GFP RPE65 PNA Lectin
GFP GS-6 Phalloidin
1
2
3
4
5

Fig. 6

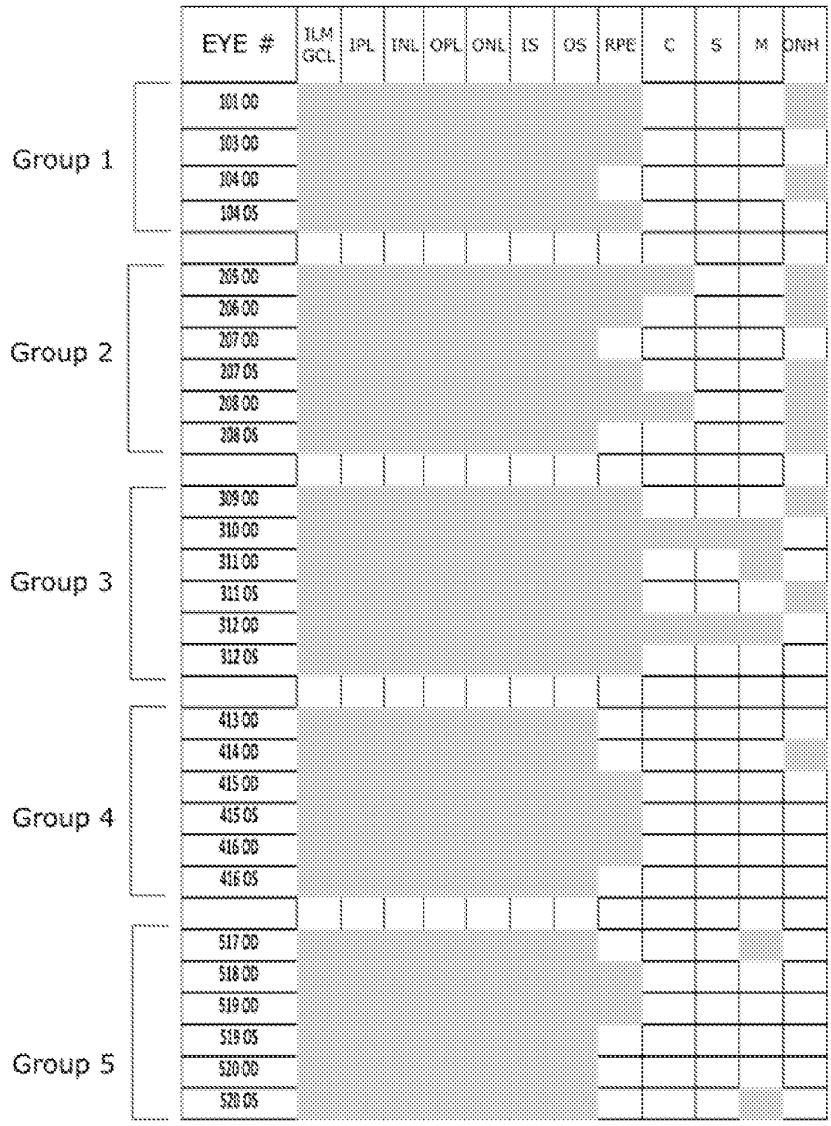

EYE #
ILM GCL
IPL
INL
OPL
ONL
IS
OS
RPE
C
S
M
ONH
Group 1
101 OD
103 OD
104 OD
104 OS
Group 2
205 OD
206 OD
207 OD
207 OS
208 OD
208 OS
Group 3
309 OD
310 OD
311 OD
311 OS
312 OD
312 OS
Group 4
413 OD
414 OD
415 OD
415 OS
416 OD
416 OS
Group 5
517 OD
518 OD
519 OD
519 OS
520 OD
520 OS

Fig. 7

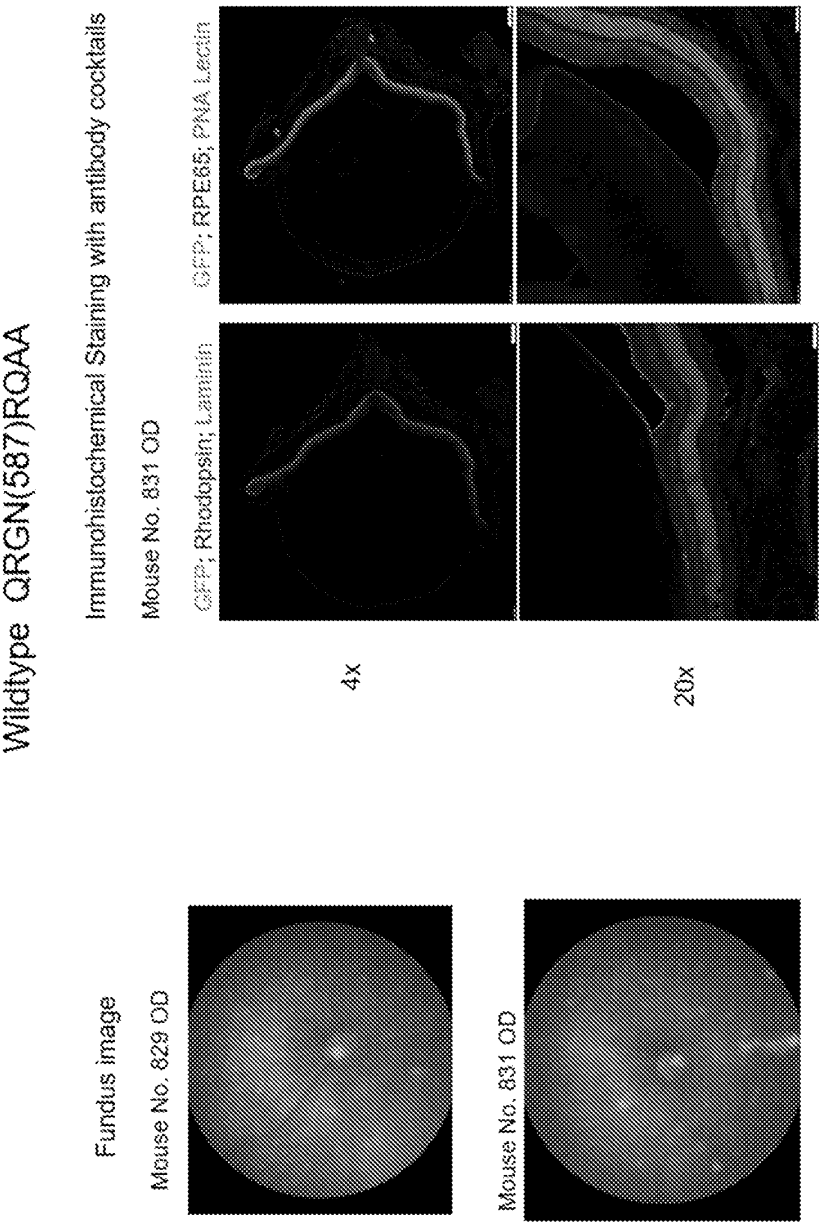

Wildtype QRGN(587)ROAA
Immunohistochemical Staining with antibody cocktails
Fundus image
Mouse No. 829 OD
Mouse No. 831 OD
Mouse No. 831 OD
GFP; Rhodopsin; Laminin
GFP; RPE65; PNA Lectin
4x
20x
Exposure length in second (S) or milli seconds (MS)
DAPI: 125 ms
GFP: 300 ms
Rhodopsin: 750 ms
Laminin: 1 s
DAPI: 10 ms
GFP: 30 ms
Rhodopsin: 750 ms
Laminin: 600 ms

Fig. 8

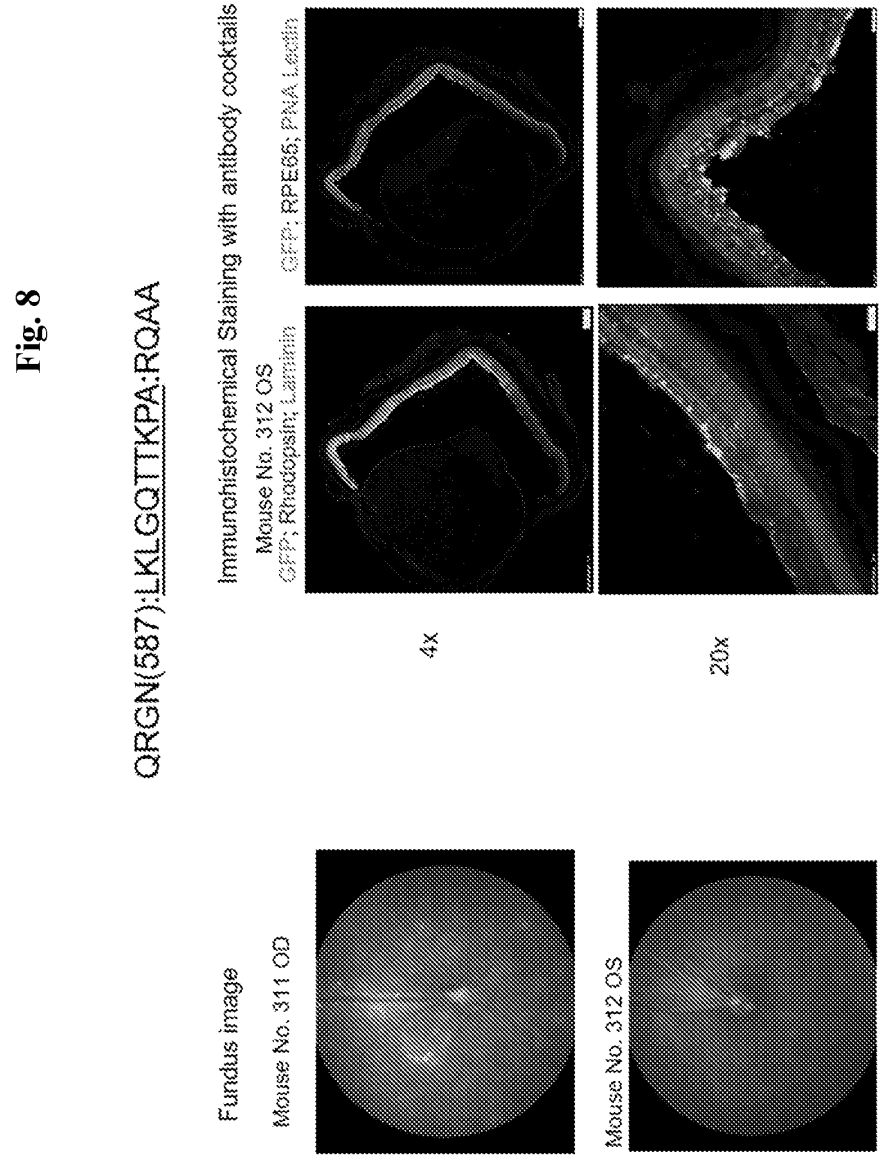
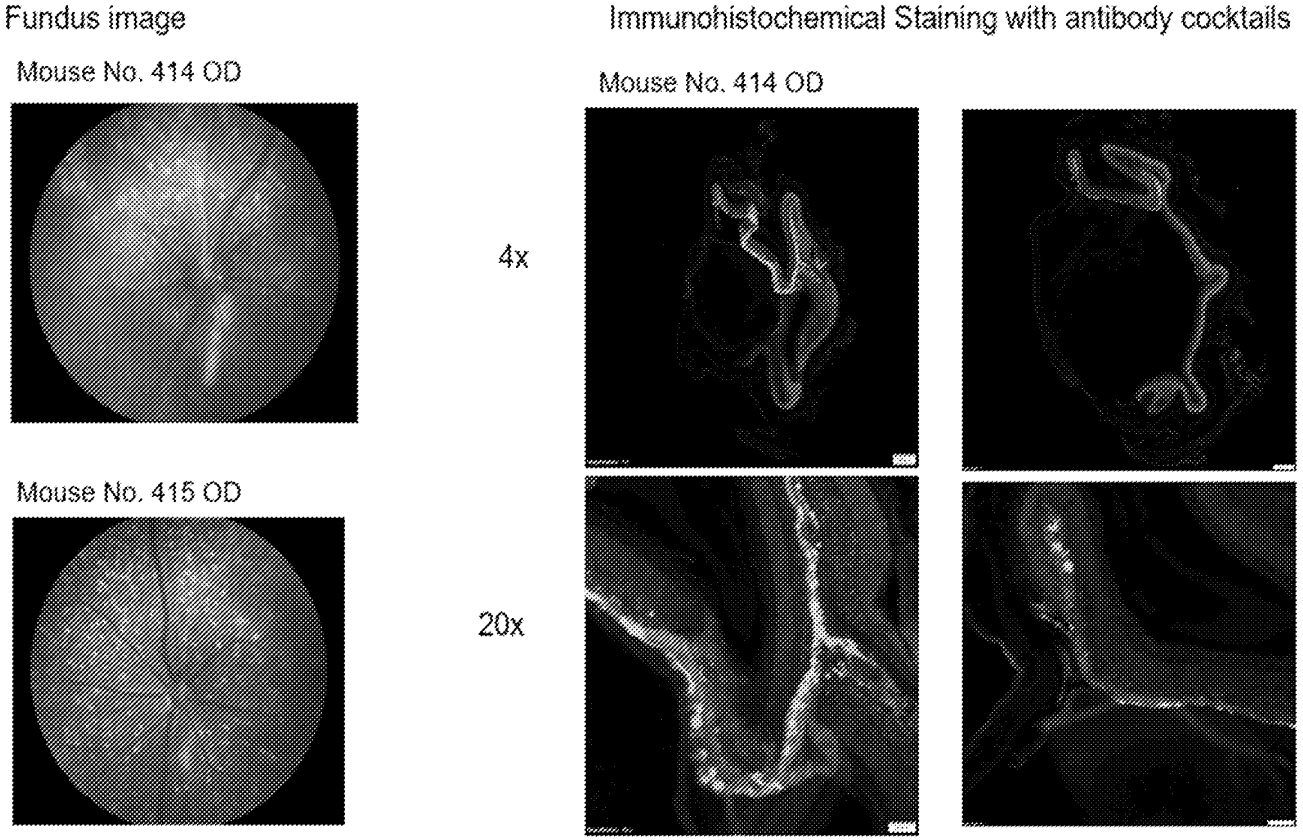

QRGN(587):LKLGQTTKPA:RQAA
Fundus image
Mouse No. 311 OD
Mouse No. 312 OS
Immunohistochemical Staining with antibody cocktails
Mouse No. 312 OS
GFP; Rhodopsin; Laminin
GFP; RPE65; PNA Lectin
4x
20x
Exposure length in second (s) or milli seconds (MS)
DAPI: 125 ms
GFP: 300 ms
Rhodopsin: 750 ms
Laminin: 1 s
DAPI: 10 ms
GFP: 30 ms
Rhodopsin: 750 ms
Laminin: 500 ms

Fig. 9

QRGN(587):LALGQTTKPA:RQAA



Exposure length in second (S) or milli seconds (MS)

- DAPI: 125 ms
- GFP: 300 ms
- Rhodopsin: 750 ms
- Laminin: 1 s

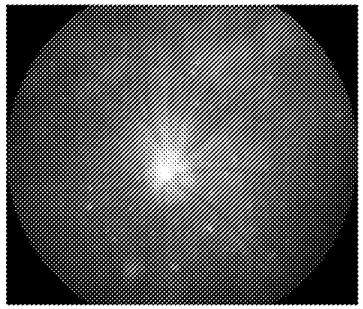
- DAPI: 10 ms
- GFP: 30 ms
- Rhodopsin: 750 ms
- Laminin: 500 ms

Fig. 10

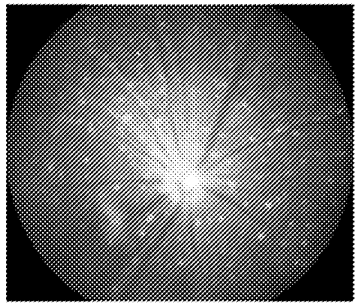
TPSG(453):LALGETTRPA:TTTQ

Fundus image

Mouse No. 208 OD

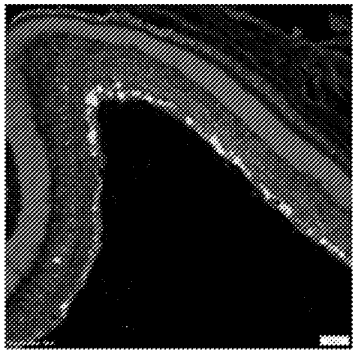


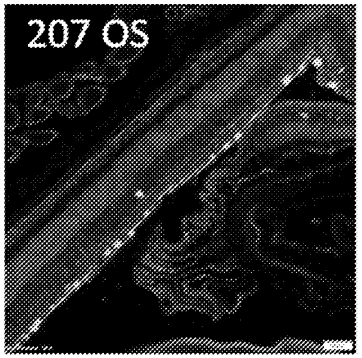
Mouse No. 206 OD



Immunohistochemical Staining with antibody cocktails

Mouse No. 205 OD





Exposure length in second (S) or milli seconds (MS)

- DAPI: 125 ms
- GFP: 300 ms
- Rhodopsin: 750 ms
- Laminin: 1 s

- DAPI: 10 ms
- GFP: 30 ms
- Rhodopsin: 750 ms
- Laminin: 500 ms

Fig. 11

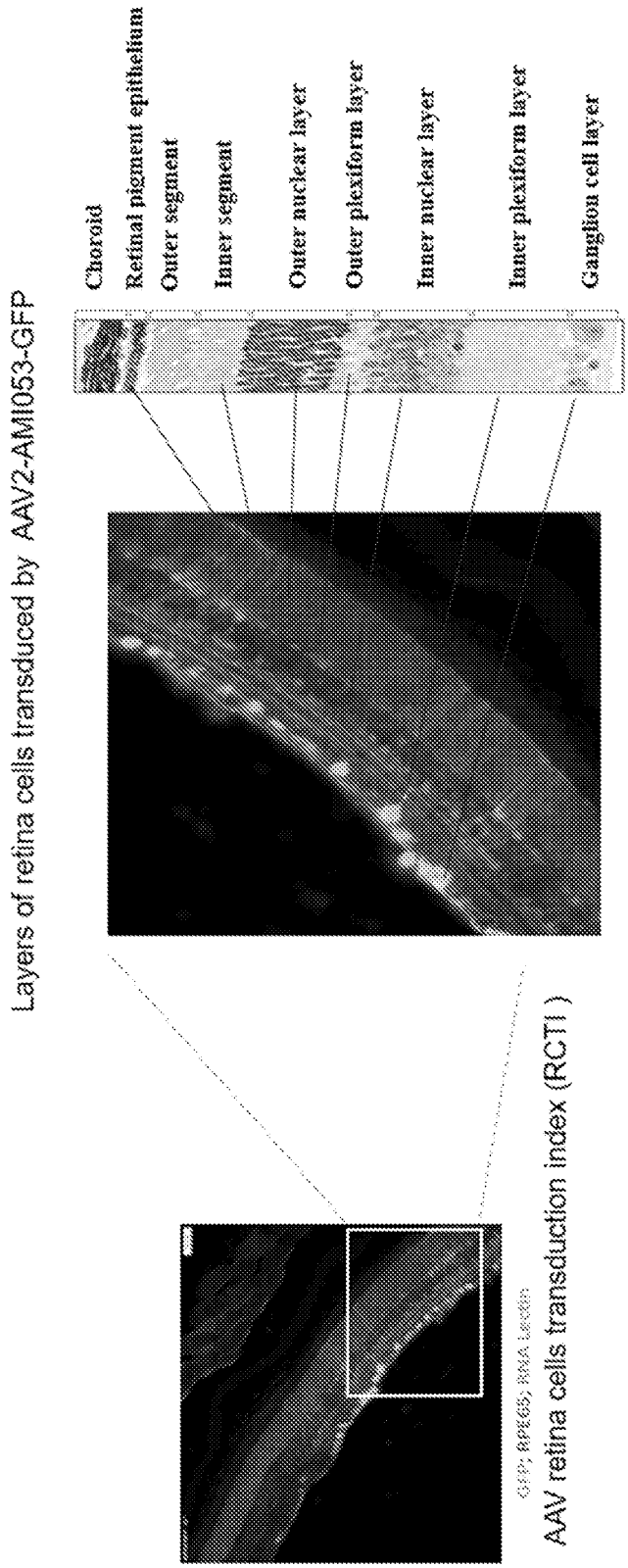

Layers of retina cells transduced by AAV2-AMI053-GFP
Choroid
Retinal pigment epithelium
Outer segment
Inner segment
Outer nuclear layer
Outer plexiform layer
Inner nuclear layer
Inner plexiform layer
Ganglion cell layer
AAV retina cells transduction index (RCTI)

Fig. 12

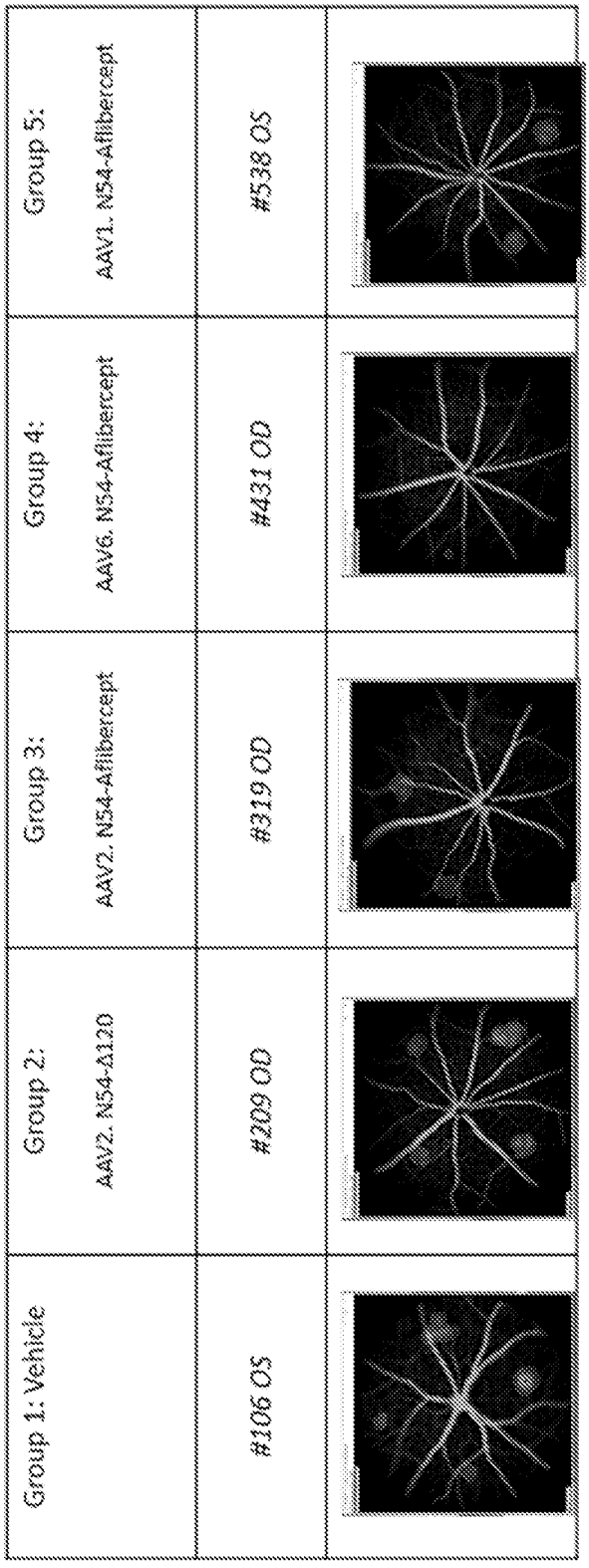

Group 1: Vehicle
Group 2: AAV2. N54-Δ120
Group 3: AAV2. N54-Aflibercept
Group 4: AAV6. N54-Aflibercept
Group 5: AAV1. N54-Aflibercept
#106 OS
#209 OD
#319 OD
#431 OD
#538 OS
OS=left eye
OD=Right eye

Fig. 13B

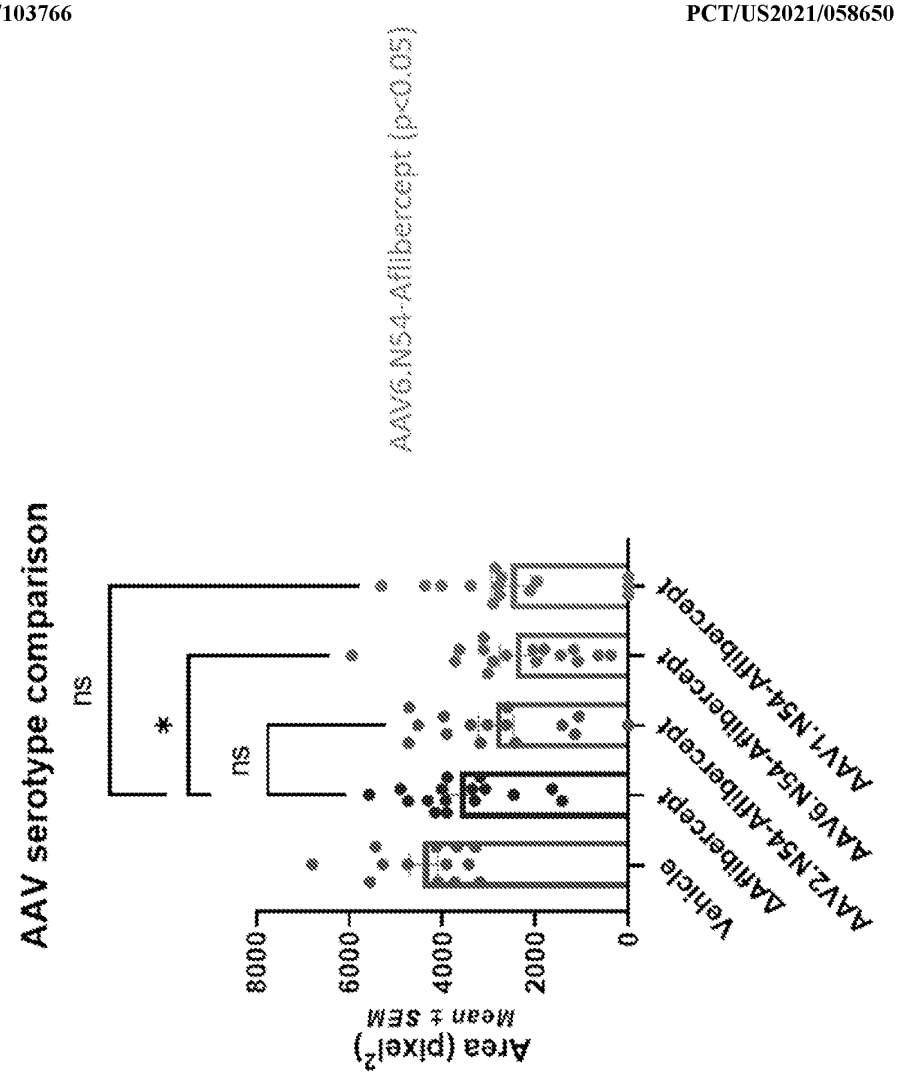


Fig. 13A

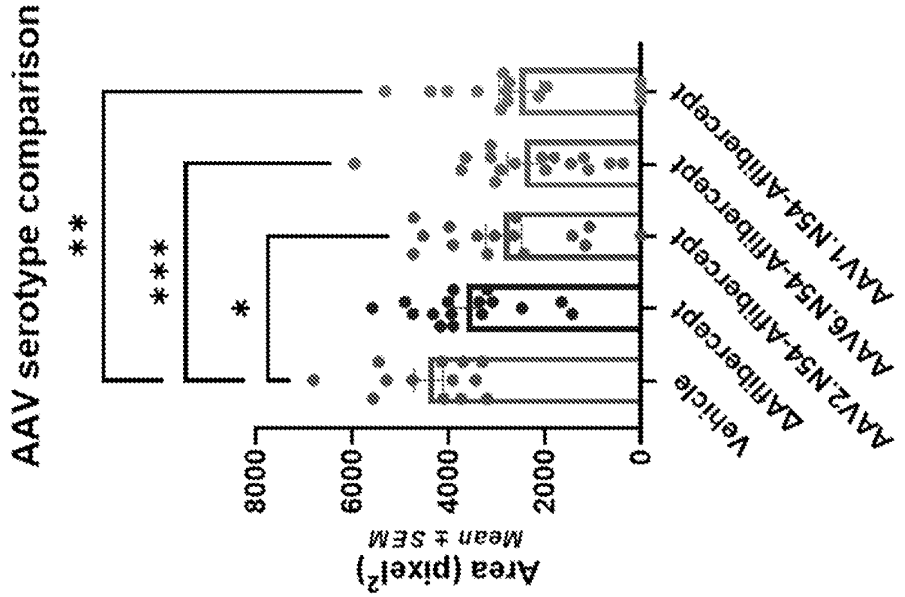


Fig. 14

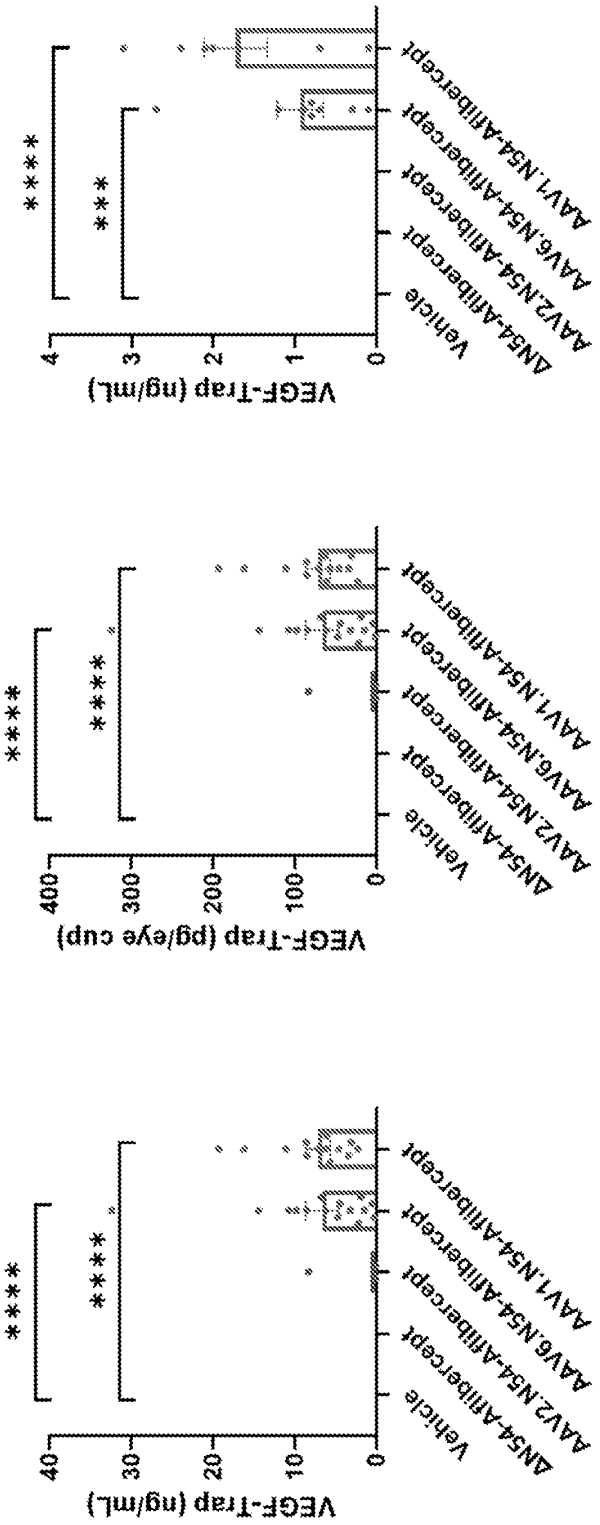
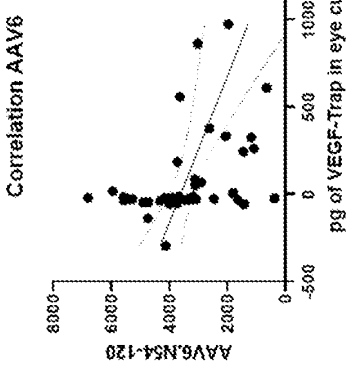
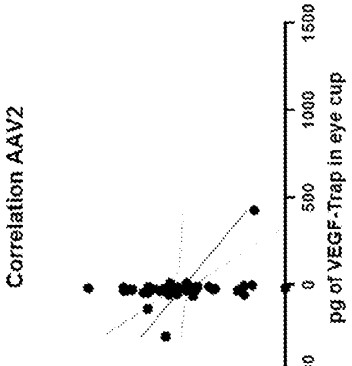

VEGF-Trap (ng/mL)
0
10
20
30
40
****
****
Vehicle
ΔN54-Aflibercept
AAV2.N54-Aflibercept
AAV6.N54-Aflibercept
AAV1.N54-Aflibercept
VEGF-Trap (pg/eye cup)
0
100
200
300
400
****
****
Vehicle
ΔN54-Aflibercept
AAV2.N54-Aflibercept
AAV6.N54-Aflibercept
AAV1.N54-Aflibercept
VEGF-Trap (ng/mL)
0
1
2
3
4
****
***
Vehicle
ΔN54-Aflibercept
AAV2.N54-Aflibercept
AAV6.N54-Aflibercept
AAV1.N54-Aflibercept

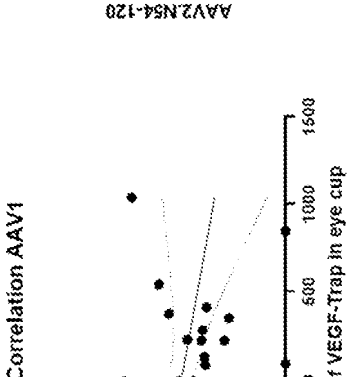
Fig. 15



Pearson r	AAV1.N54-120
r	-0.1854
95% confidence interval	-0.4601 to 0.1218
R squared	0.03436
P value	
P (two-tailed)	0.2340
P value summary	ns
Significant? (alpha = 0.05)	No



Pearson r	AAV2.N54-120
r	-0.3100
95% confidence interval	-0.5557 to -0.01441
R squared	0.09608
P value	
P (two-tailed)	0.0406
P value summary	*
Significant? (alpha = 0.05)	Yes



Pearson r	AAV6.N54-120
r	-0.4135
95% confidence interval	-0.6305 to -0.1366
R squared	0.1710
P value	
P (two-tailed)	0.0047
P value summary	**
Significant? (alpha = 0.05)	Yes

Fig. 16

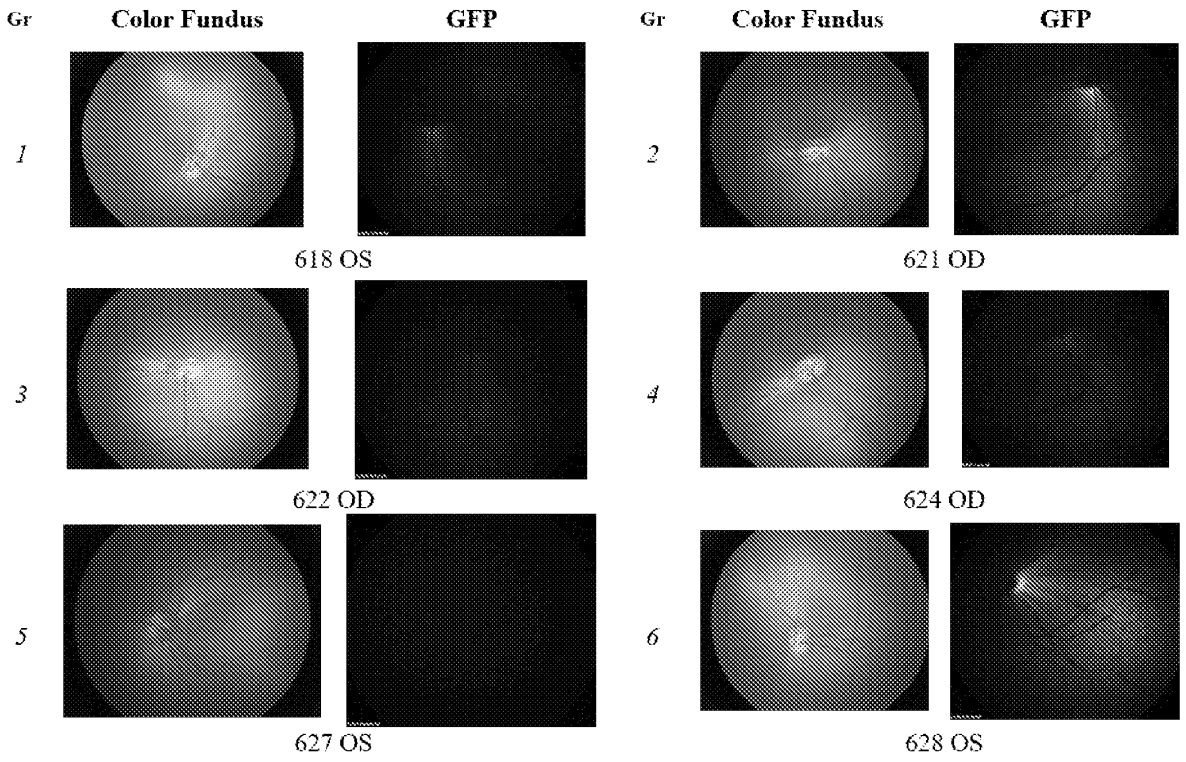

Gr
Color Fundus
GFP
1
618 OS
Gr
Color Fundus
GFP
2
621 OD
3
622 OD
4
624 OD
5
627 OS
6
628 OS

Fig. 17

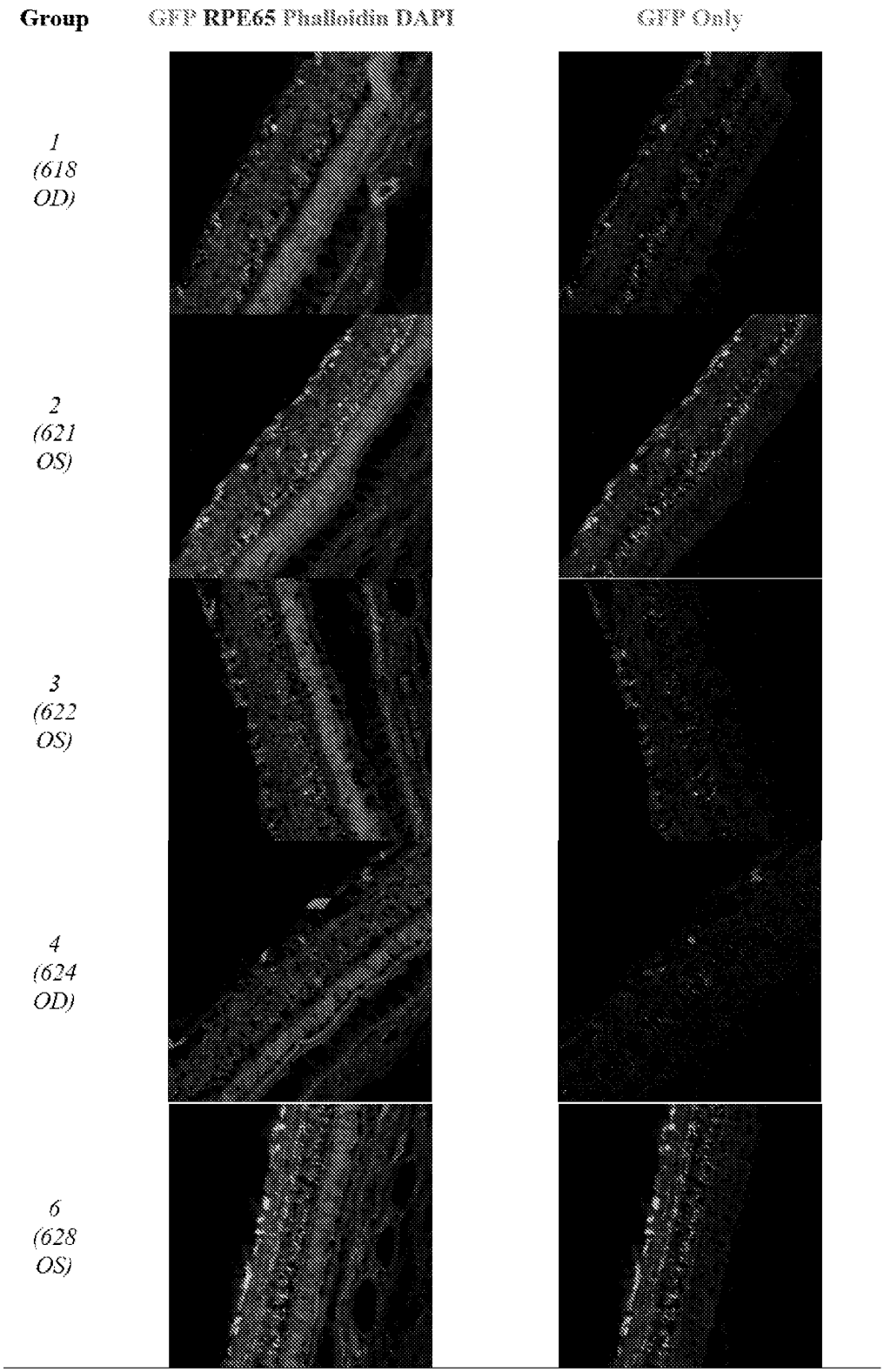

Group
GFP RPE65 Phalloidin DAPI
GFP Only
1 (618 OD)
2 (621 OS)
3 (622 OS)
4 (624 OD)
6 (628 OS)

Fig. 18

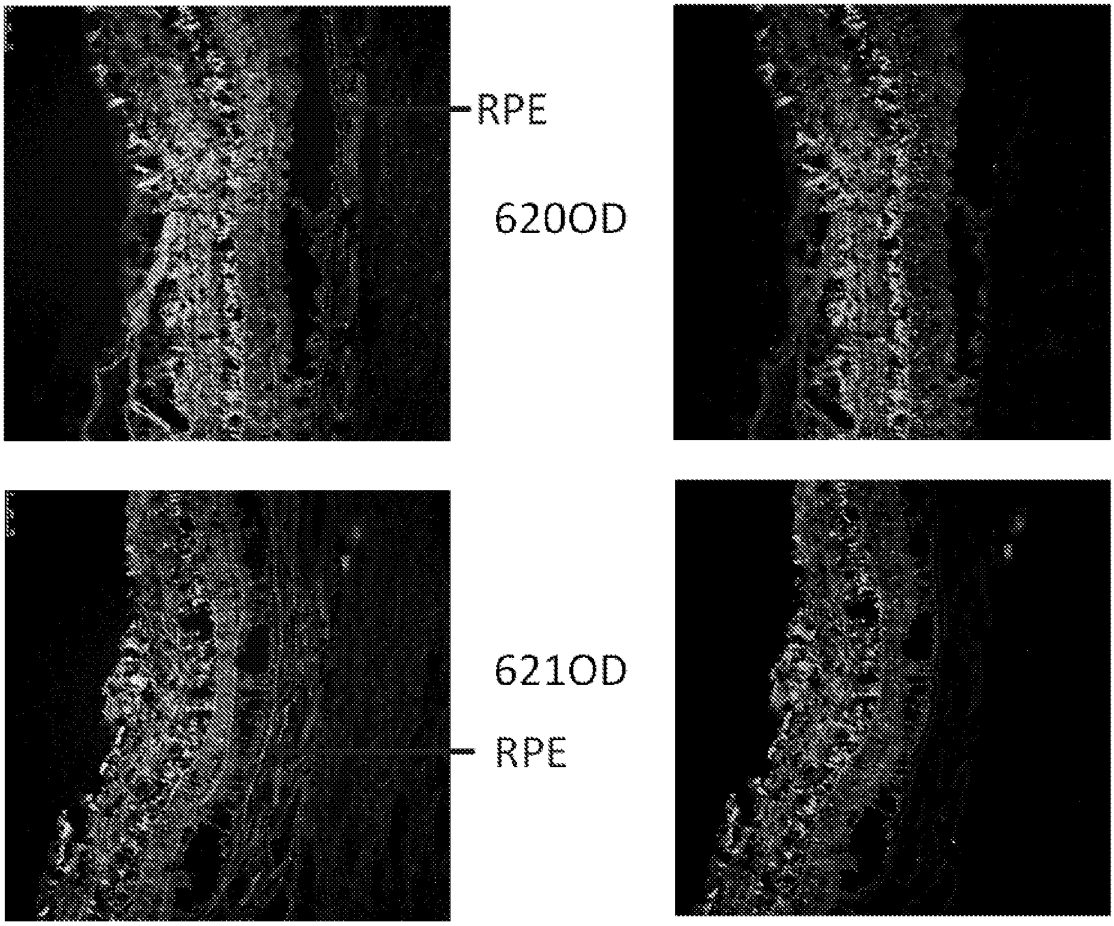


Fig. 19A

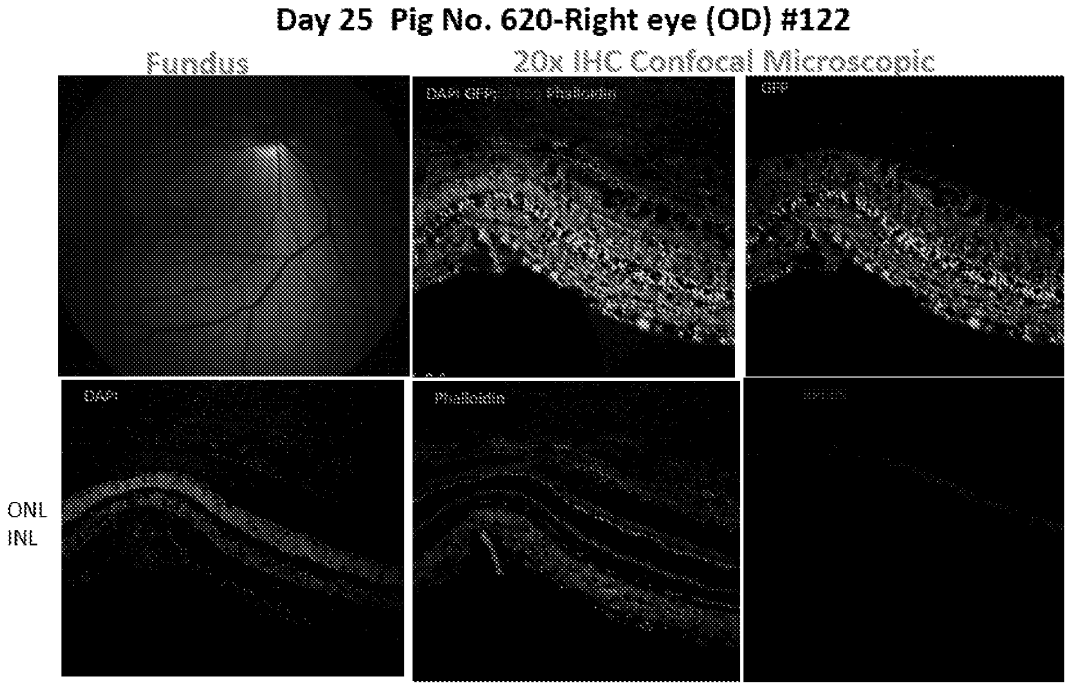

Day 25 Pig No. 620-Right eye (OD) #122
Fundus
20x IHC Confocal Microscopic
DAPI GFP Phalloidin
GFP
DAPI
Phalloidin
ONL
INL

Fig. 19B

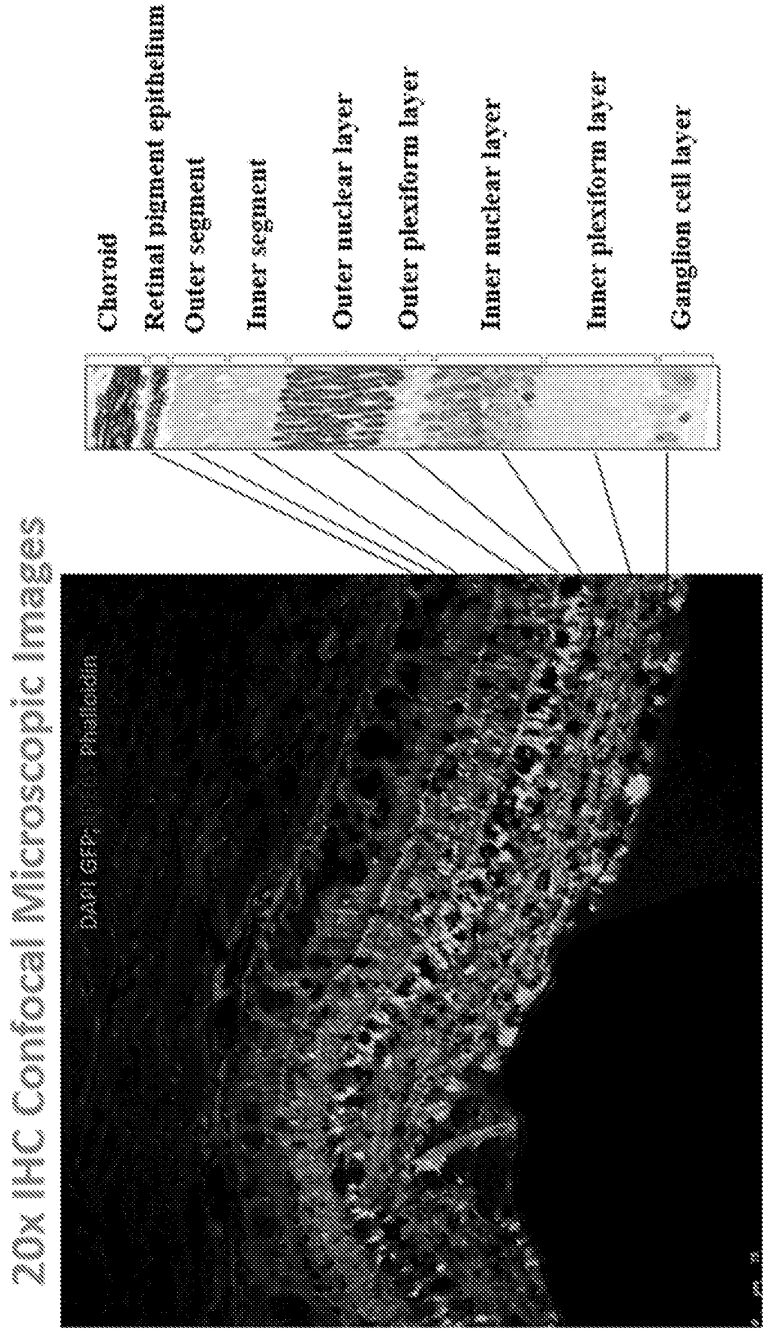
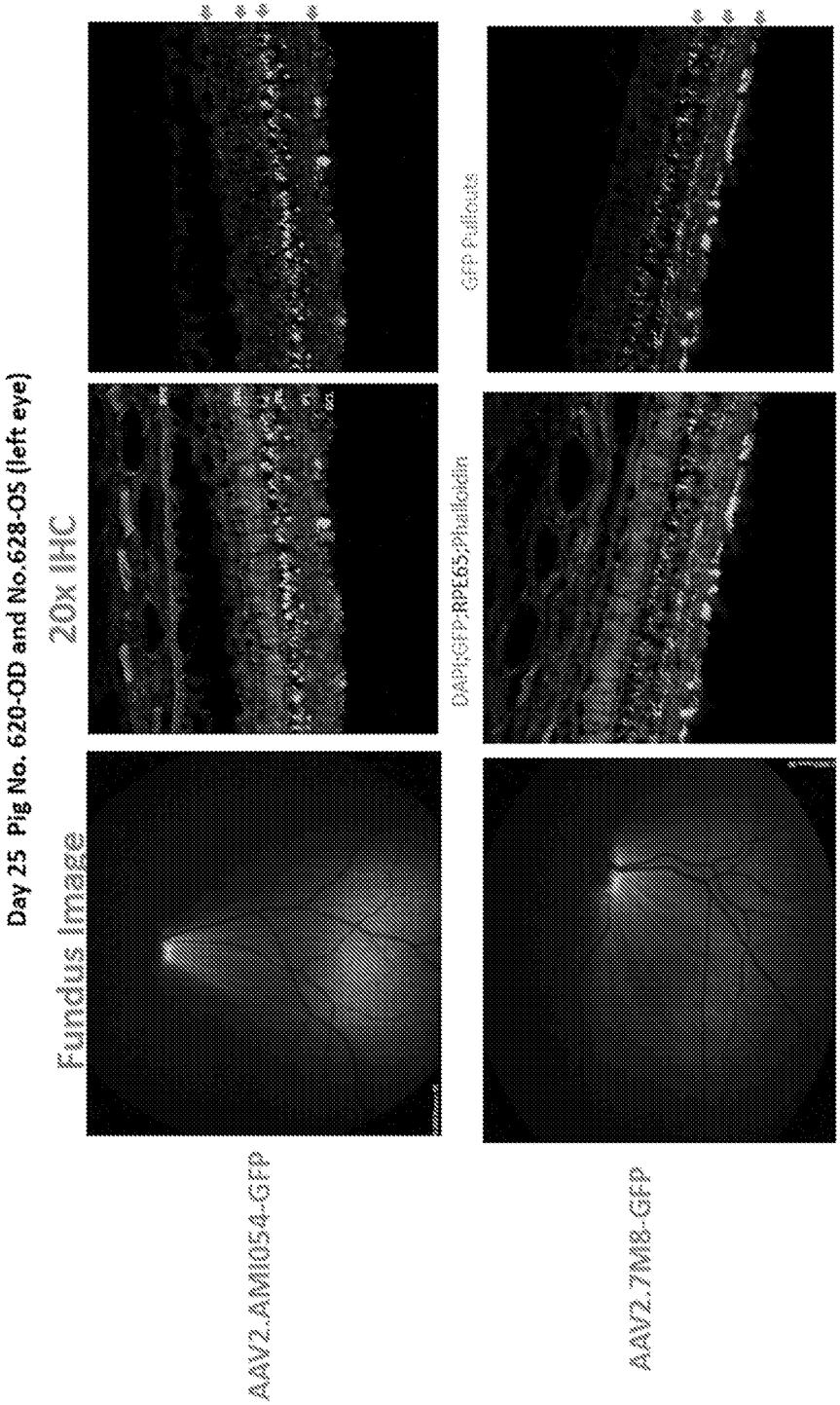

Day 25 Pig No. 620-right eye
20x IHC Confocal Microscopic Images
DAPI GFP Phalloidin
Choroid
Retinal pigment epithelium
Outer segment
Inner segment
Outer nuclear layer
Outer plexiform layer
Inner nuclear layer
Inner plexiform layer
Ganglion cell layer

Fig. 20


Day 25 Pig No. 620-OD and No.628-OS (left eye)
Fundus image
20x IHC
DAPI/GFP/RPE65/Phalloidin
GFP Fulllouts
AAV2.AM1054-GFP
AAV2.7M8-GFP