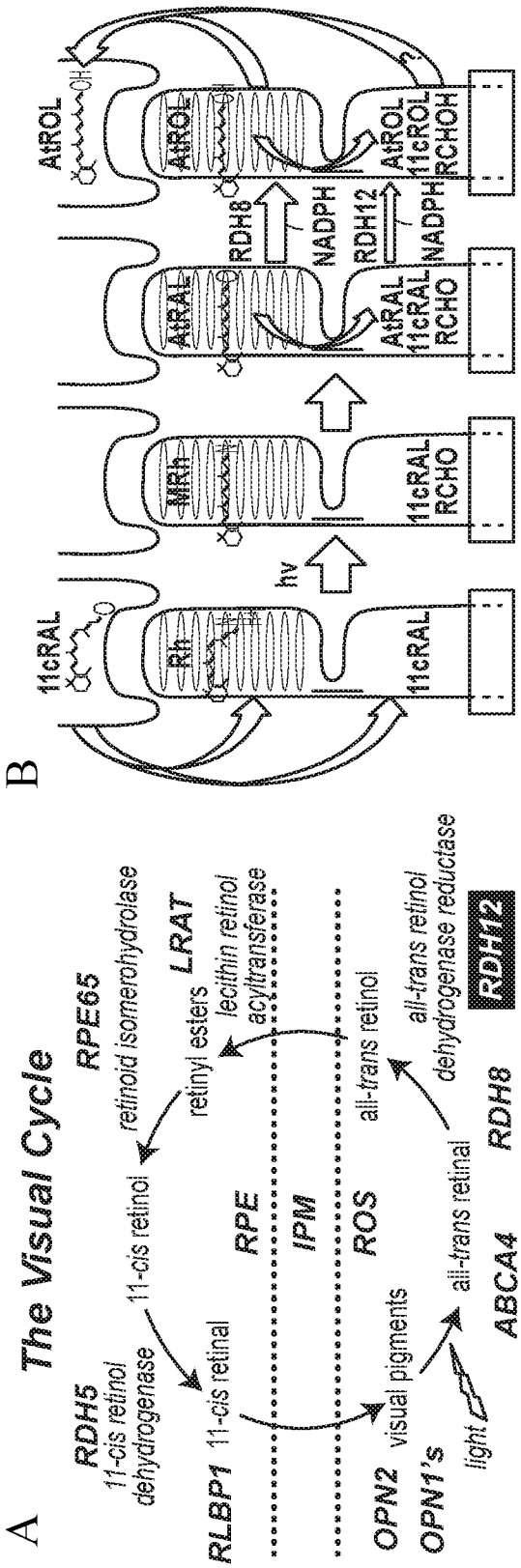

A
The Visual Cycle
RDH5
11-cis retinol dehydrogenase
RLBP1
11-cis retinal
OPN2
OPN1's
visual pigments
light
11-cis retinol
RPE65
retinoid isomerohydrolase
retinyl esters
LRAT
lecithin retinol acyltransferase
RPE
IPM
ROS
all-trans retinol
all-trans retinal
ABCA4
RDH8
all-trans retinol dehydrogenase reductase
RDH12
B
11cRAL
Rh
11cRAL
hv
MRh
11cRAL
RCHO
AtRAL
RDH8
NADPH
AtROL
AtRAL
11cRAL
RCHO
RDH12
NADPH
AtROL
11cROL
RCHOH
AtROL

Figure 1

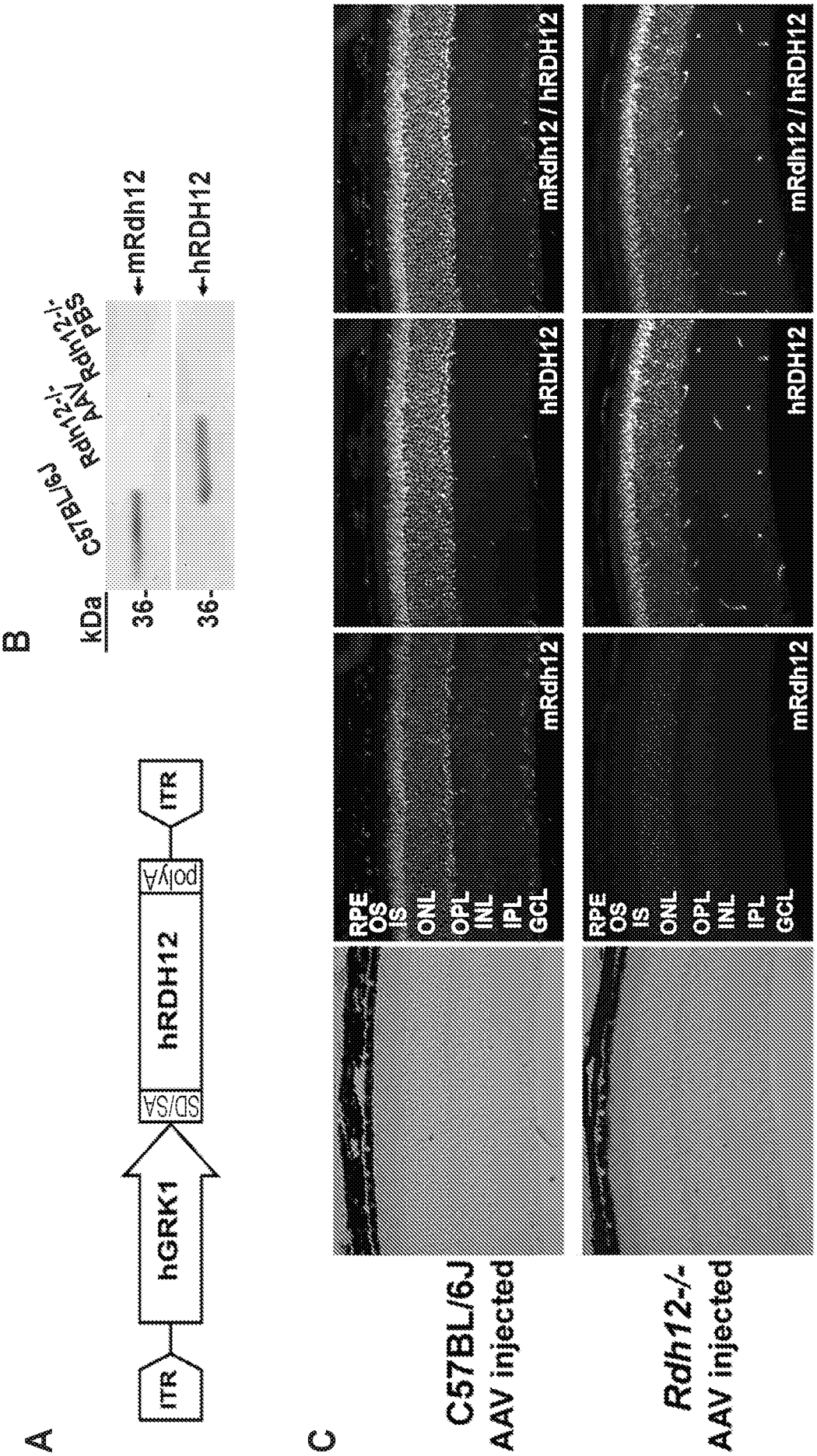

A
ITR
hGRK1
SD/SA
hRDH12
polyA
ITR
B
kDa
C57BL/6J
Rdh12-/- AAV Rdh12 pBS
36-
36-
←mRdh12
←hRDH12
C
C57BL/6J
AAV injected
Rdh12-/-
AAV injected
RPE
OS
IS
ONL
OPL
INL
IPL
GCL
mRdh12
hRDH12
mRdh12 / hRDH12

Figure 2

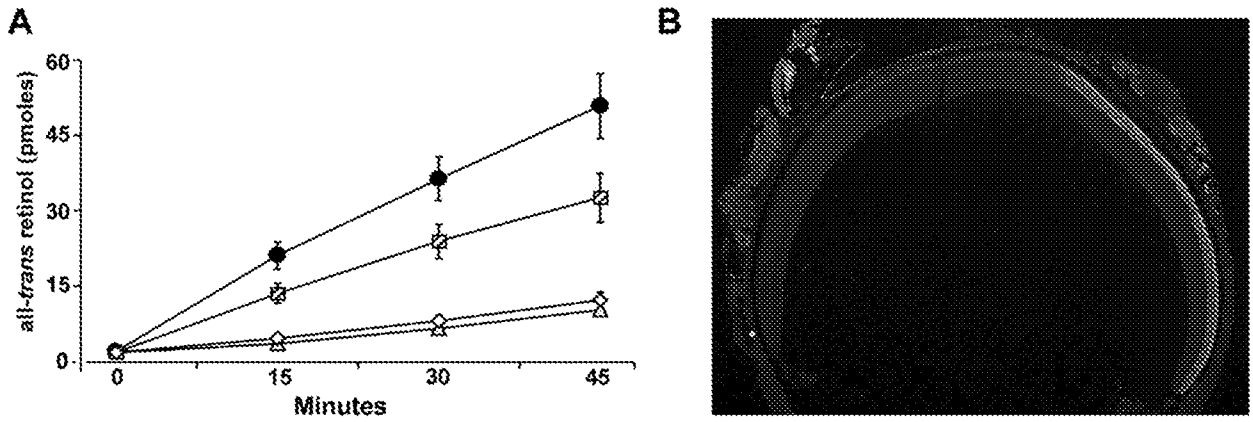


Figure 3

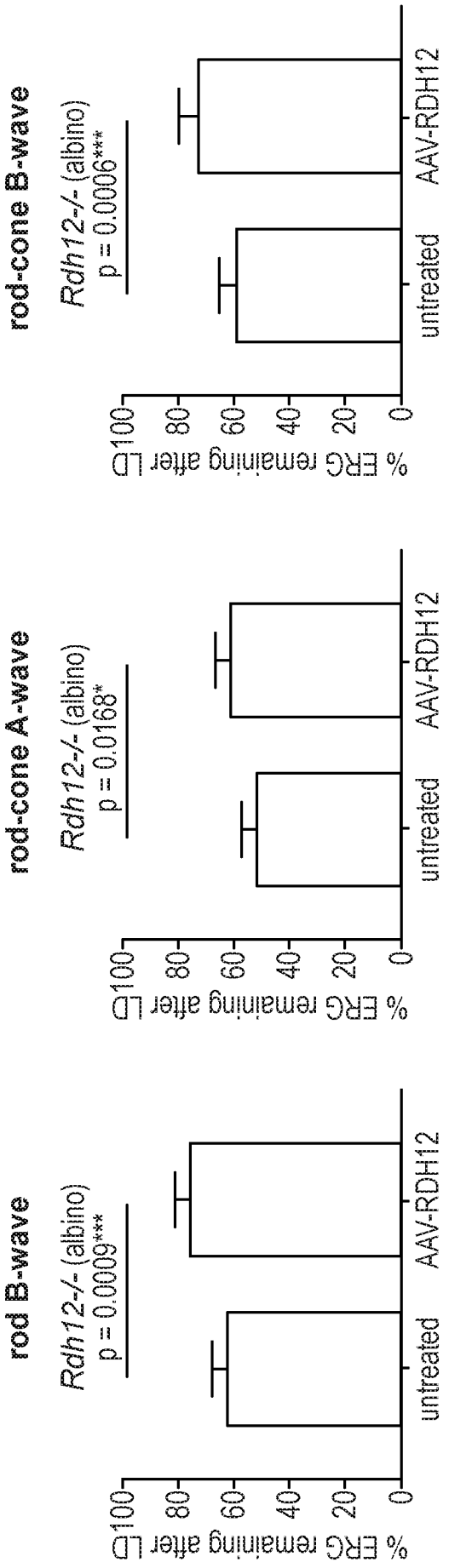

rod B-wave
Rdh12-/- (albino)
p = 0.0009***
% ERG remaining after LD
100
80
60
40
20
0
untreated
AAV-RDH12
rod-cone A-wave
Rdh12-/- (albino)
p = 0.0168*
% ERG remaining after LD
100
80
60
40
20
0
untreated
AAV-RDH12
rod-cone B-wave
Rdh12-/- (albino)
p = 0.0006***
% ERG remaining after LD
100
80
60
40
20
0
untreated
AAV-RDH12

Figure 4

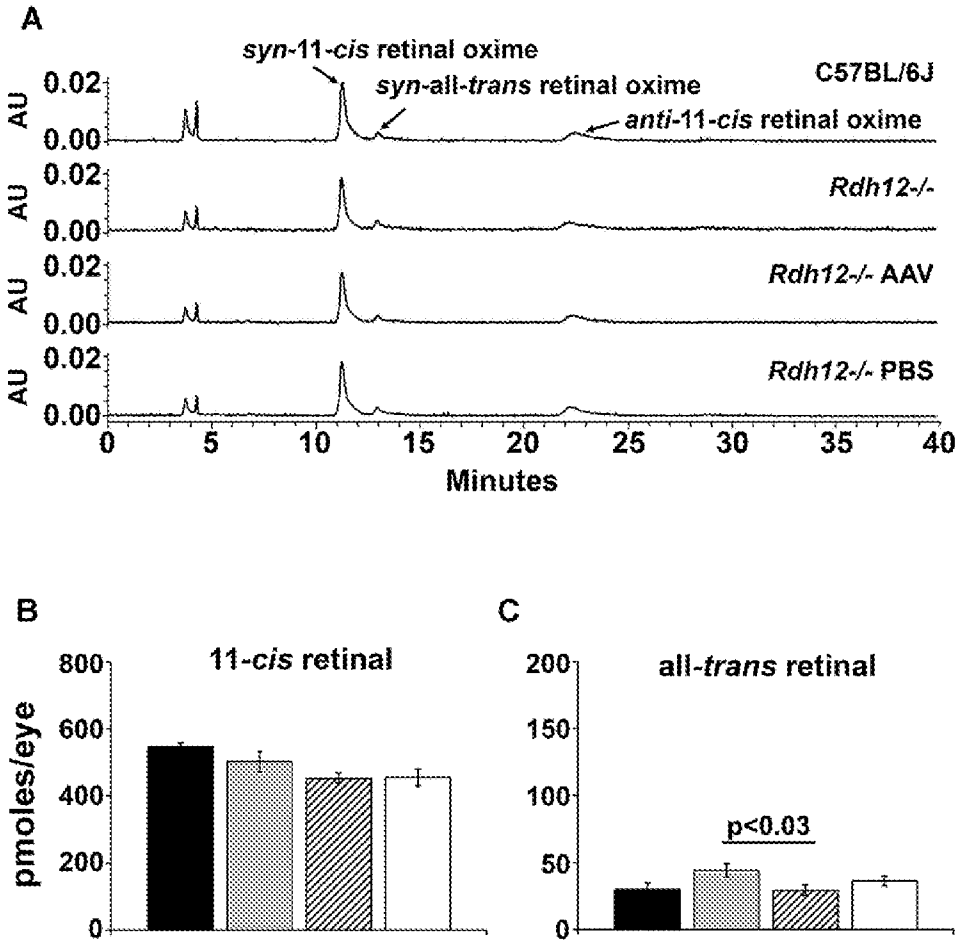

A
syn-11-cis retinal oxime
syn-all-trans retinal oxime
anti-11-cis retinal oxime
C57BL/6J
Rdh12-/-
Rdh12-/- AAV
Rdh12-/- PBS
AU
0.02
0.00
0
5
10
15
20
25
30
35
40
Minutes
B
11-cis retinal
pmoles/eye
800
600
400
200
0
C
all-trans retinal
200
150
100
50
0
p<0.03

Figure 5

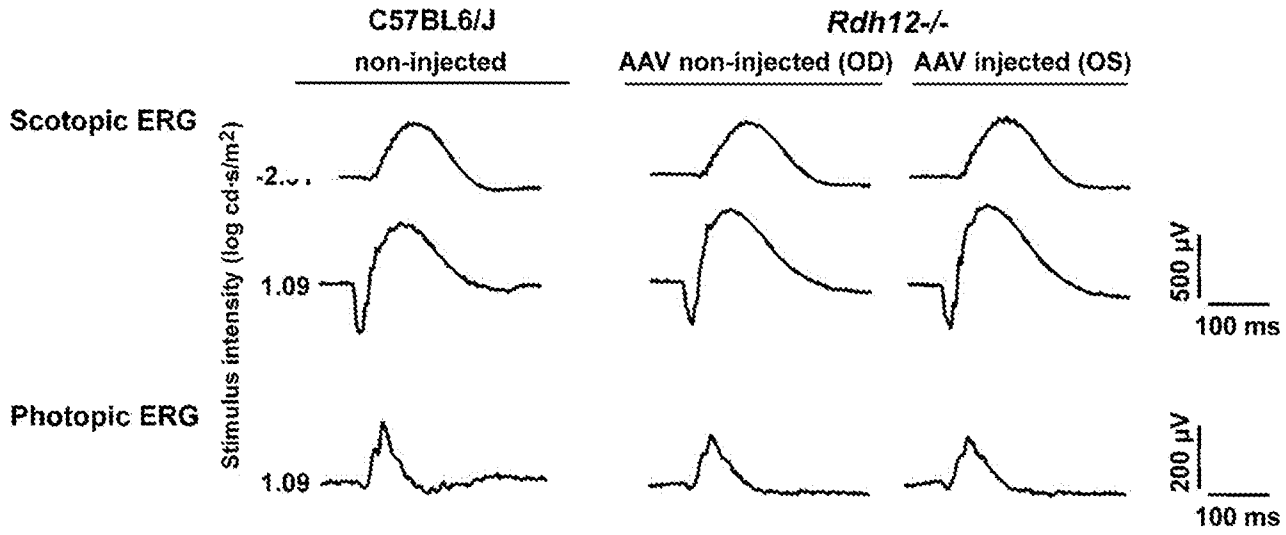

C57BL6/J
non-injected
Rdh12-/-
AAV non-injected (OD)
AAV injected (OS)
Scotopic ERG
Photopic ERG
Stimulus intensity (log cd-s/m2)
1.09
1.09
500 µV
100 ms
200 µV
100 ms

Figure 6

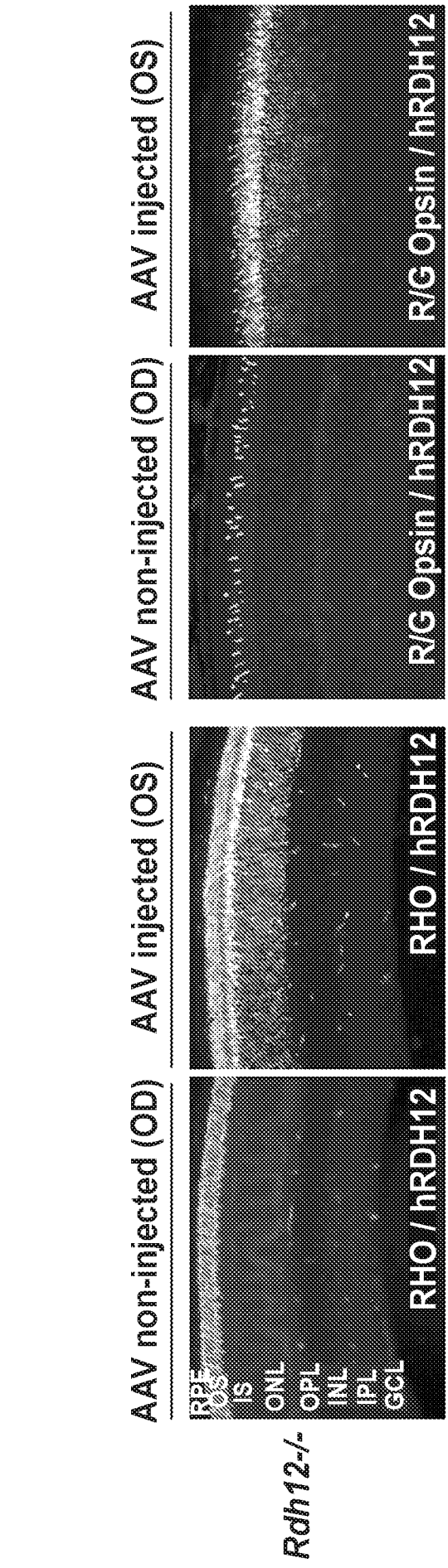

AAV non-injected (OD)
AAV injected (OS)
AAV non-injected (OD)
AAV injected (OS)
Rdh12-/-
RPE
OS
IS
ONL
OPL
INL
IPL
GCL
RHO / hRDH12
RHO / hRDH12
R/C Opsin / hRDH12
R/C Opsin / hRDH12

Figure 7

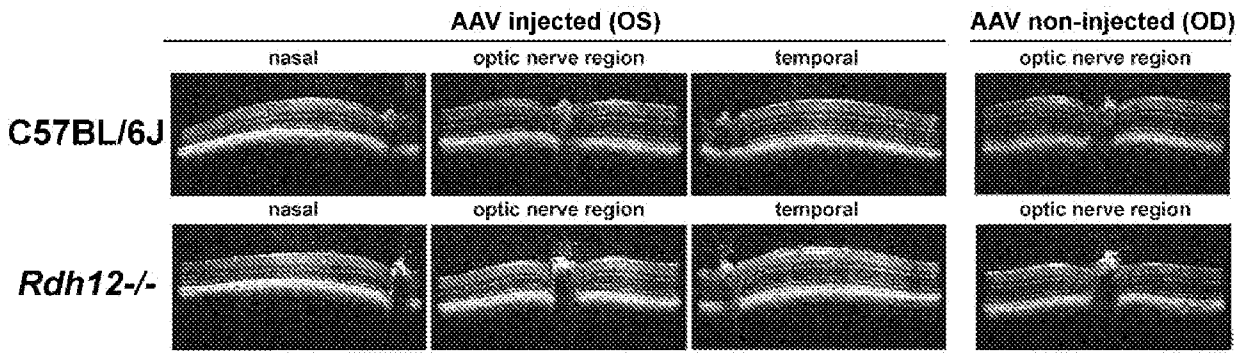

AAV injected (OS)
AAV non-injected (OD)
nasal
optic nerve region
temporal
optic nerve region
C57BL/6J
nasal
optic nerve region
temporal
optic nerve region
Rdh12-/-

Figure 8

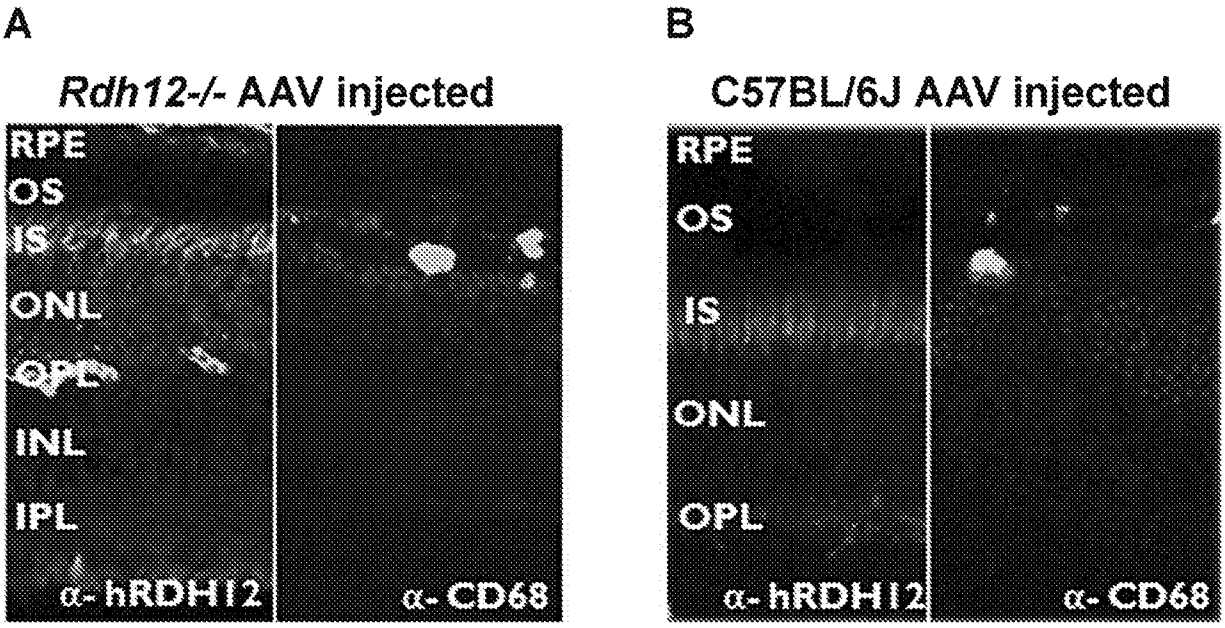

A
Rdh12-/- AAV injected
RPE
OS
IS
ONL
OPL
INL
IPL
α- hRDH12
α- CD68
B
C57BL/6J AAV injected
RPE
OS
IS
ONL
OPL
α- hRDH12
α- CD68

Figure 9