A
REST
N
C
RZFD
N-terminal repression domain
DNA binding domain
C-terminal repression domain
RZFD-V1
RZFD
DNA binding domain
RZFD-V2
VP64
RZFD
DNA binding domain
RZFD-V3
P65
HSF1
RZFD
DNA binding domain
RZFDmax
bpNLS
RZFD
bpNLS
DNA binding domain
B
N-terminal repression domain
C-terminal repression domain
DNA binding domain
Repression complex
Repression complex
RE1/NRSE
Neuronal gene slience
In Astrocyte
C
N-terminal repression domain
C-terminal repression domain
DNA binding domain
Repression complex
Repression complex
DNA Binding Blocked
RZFD or RZFDmax
RE1/NRSE
Neuronal gene expression
Neuronal Genes
Astrocyte to Neuron Conversion
D
N-terminal repression domain
C-terminal repression domain
DNA binding domain
Repression complex
Repression complex
DNA Binding Blocked
VP64
RZFD
RE1/NRSE
Neuronal gene expression
Neuronal Genes
Astrocyte to Neuron Conversion
E
N-terminal repression domain
C-terminal repression domain
DNA binding domain
Repression complex
Repression complex
DNA Binding Blocked
P65
HSF1
RZFD
RE1/NRSE
Neuronal gene expression
Neuronal Genes
Astrocyte to Neuron Conversion

Fig. 1

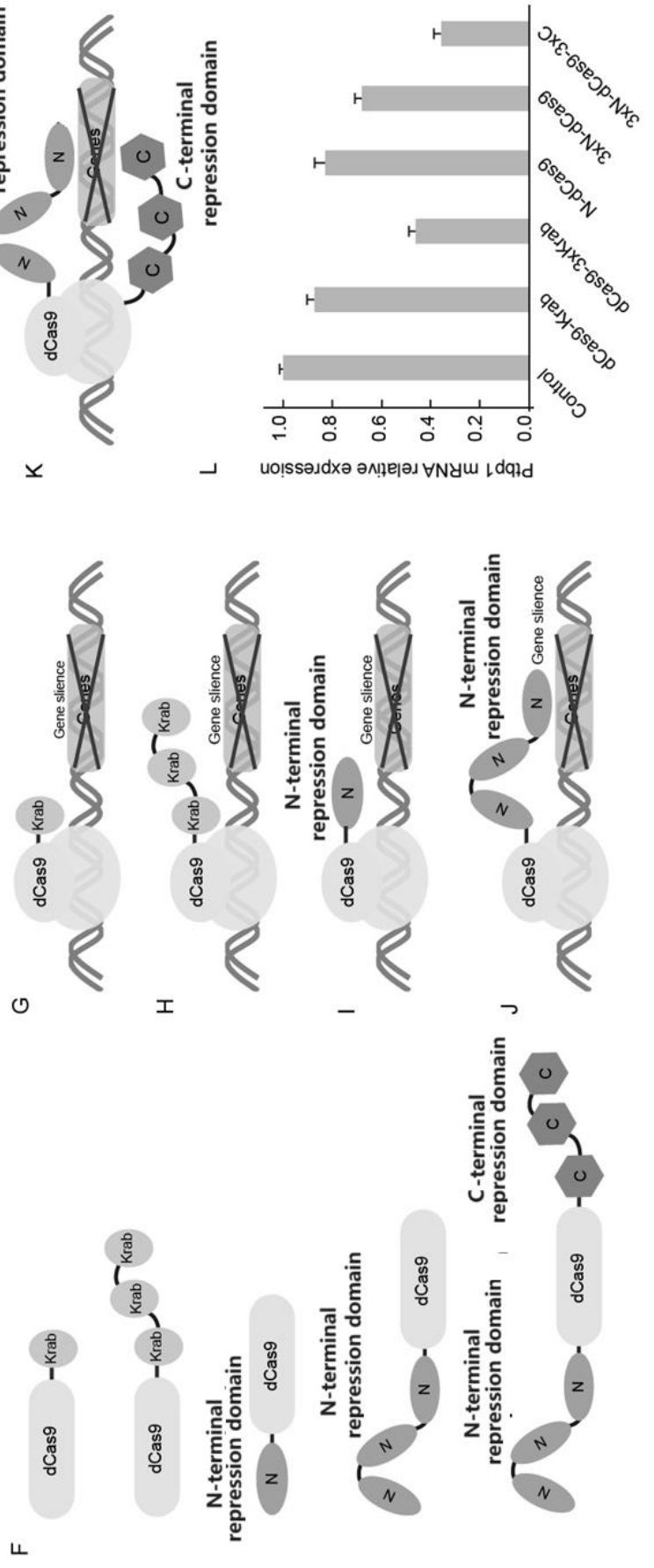


Fig. 1(continued)

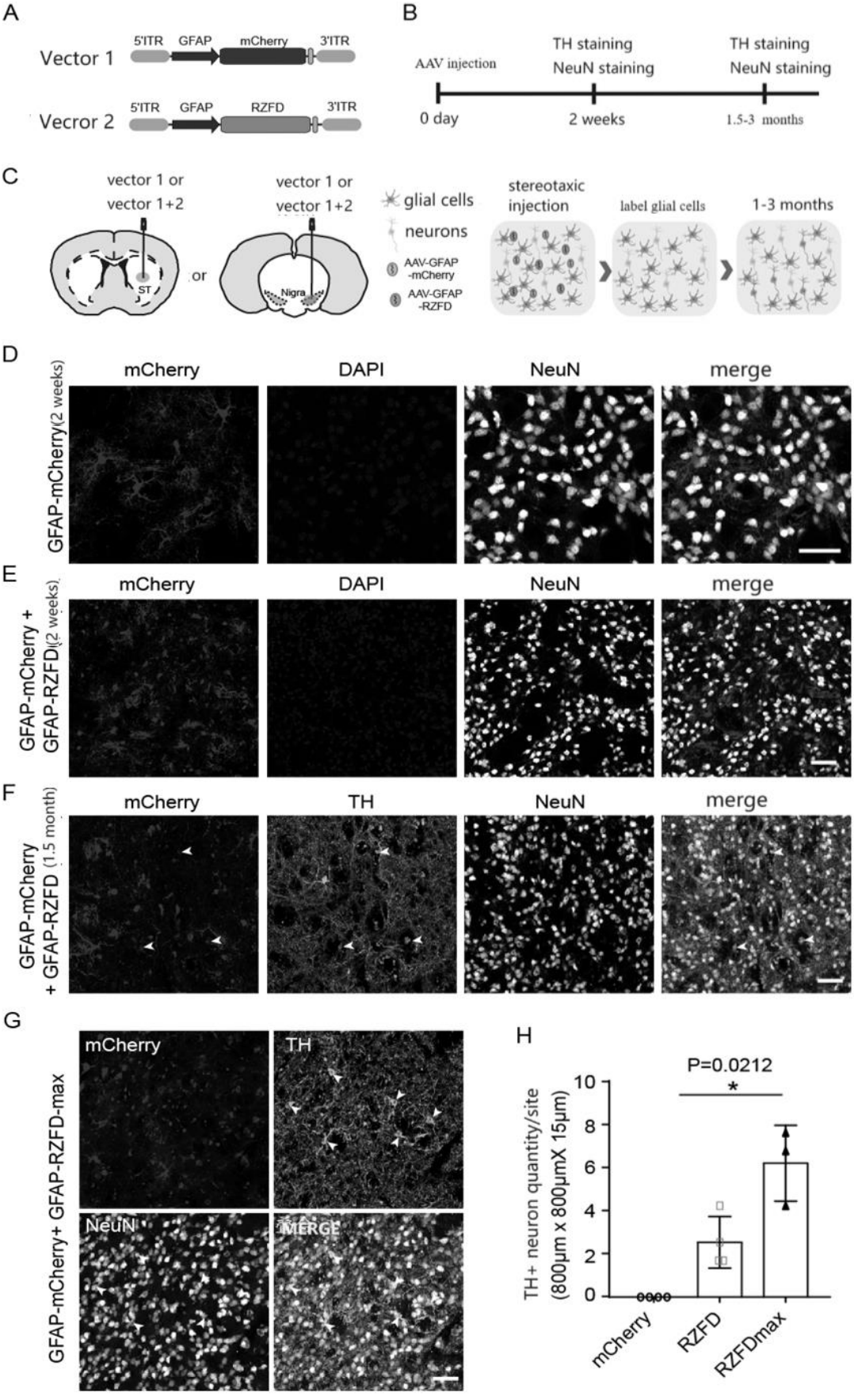

A
Vector 1
5'ITR
GFAP
mCherry
3'ITR
Vecror 2
5'ITR
GFAP
RZFD
3'ITR
B
AAV injection
TH staining
NeuN staining
TH staining
NeuN staining
0 day
2 weeks
1.5-3 months
C
vector 1 or
vector 1+2
or
vector 1 or
vector 1+2
ST
Nigra
glial cells
neurons
AAV-GFAP
-mCherry
AAV-GFAP
-RZFD
stereotaxic
injection
label glial cells
1-3 months
D
mCherry
DAPI
NeuN
merge
GFAP-mCherry(2 weeks)
E
mCherry
DAPI
NeuN
merge
GFAP-mCherry +
GFAP-RZFD(2 weeks)
F
mCherry
TH
NeuN
merge
GFAP-mCherry
+ GFAP-RZFD (1.5 month)
G
mCherry
TH
NeuN
MERGE
GFAP-mCherry+ GFAP-RZFD-max
H
P=0.0212
*
TH+ neuron quantity/site
(800μm x 800μmX 15μm)
10
8
6
4
2
0
mCherry
RZFD
RZFDmax

Fig. 2

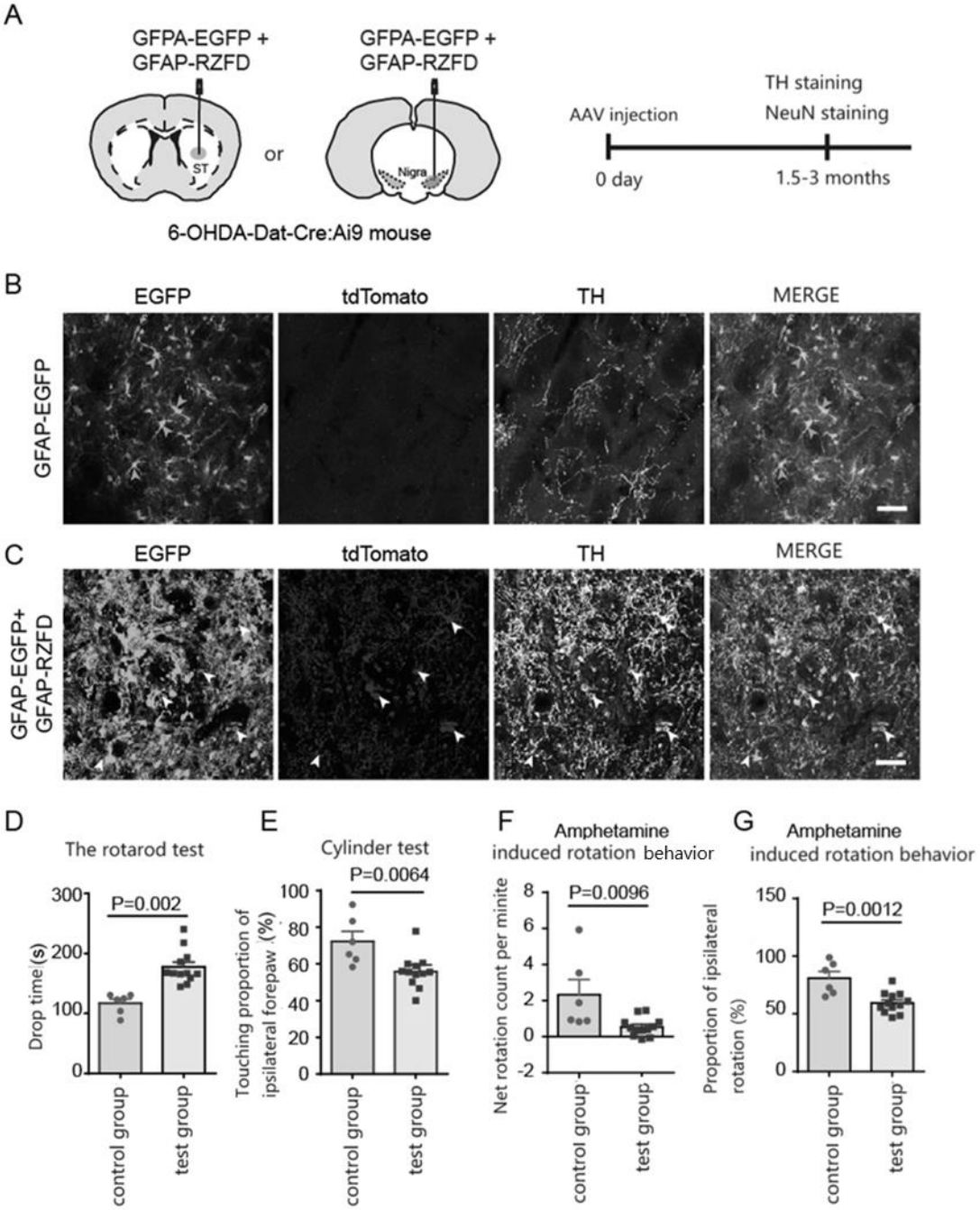

A
GFPA-EGFP +
GFAP-RZFD
GFPA-EGFP +
GFAP-RZFD
ST
or
Nigra
6-OHDA-Dat-Cre:Ai9 mouse
AAV injection
TH staining
NeuN staining
0 day
1.5-3 months
B
EGFP
tdTomato
TH
MERGE
GFAP-EGFP
C
EGFP
tdTomato
TH
MERGE
GFAP-EGFP+
GFAP-RZFD
D
The rotarod test
P=0.002
Drop time(s)
300
200
100
0
control group
test group
E
Cylinder test
P=0.0064
Touching proportion of ipsilateral forepaw (%)
100
80
60
40
20
0
control group
test group
F
Amphetamine
induced rotation behavior
P=0.0096
Net rotation count per minite
8
6
4
2
0
-2
control group
test group
G
Amphetamine
induced rotation behavior
P=0.0012
Proportion of ipsilateral rotation (%)
150
100
50
0
control group
test group

Fig. 3

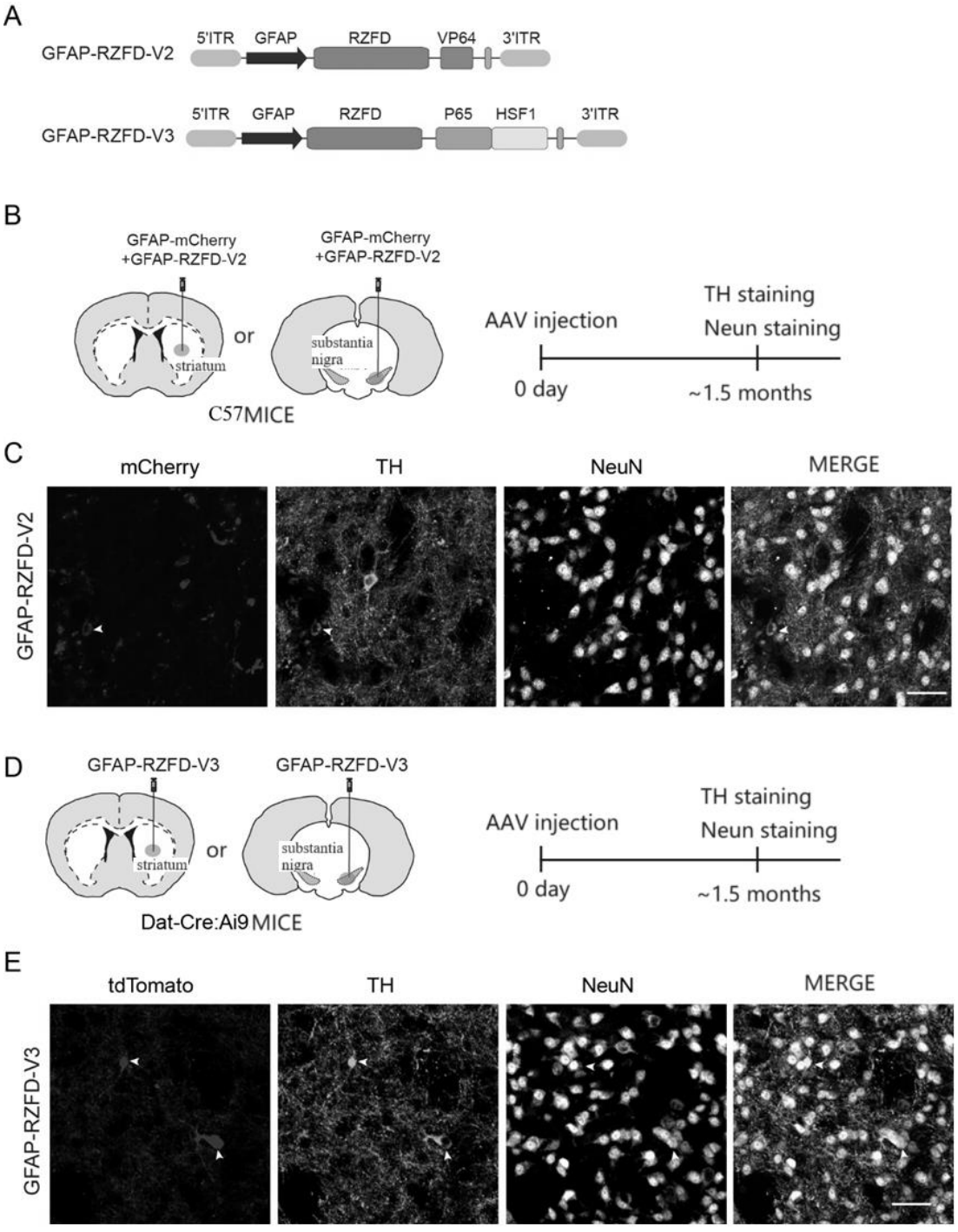

A
GFAP-RZFD-V2
5'ITR
GFAP
RZFD
VP64
3'ITR
GFAP-RZFD-V3
5'ITR
GFAP
RZFD
P65
HSF1
3'ITR
B
GFAP-mCherry
+GFAP-RZFD-V2
GFAP-mCherry
+GFAP-RZFD-V2
or
striatum
substantia
nigra
C57MICE
AAV injection
TH staining
Neun staining
0 day
~1.5 months
C
mCherry
TH
NeuN
MERGE
GFAP-RZFD-V2
D
GFAP-RZFD-V3
GFAP-RZFD-V3
or
striatum
substantia
nigra
Dat-Cre:Ai9 MICE
AAV injection
TH staining
Neun staining
0 day
~1.5 months
E
tdTomato
TH
NeuN
MERGE
GFAP-RZFD-V3

Fig. 4

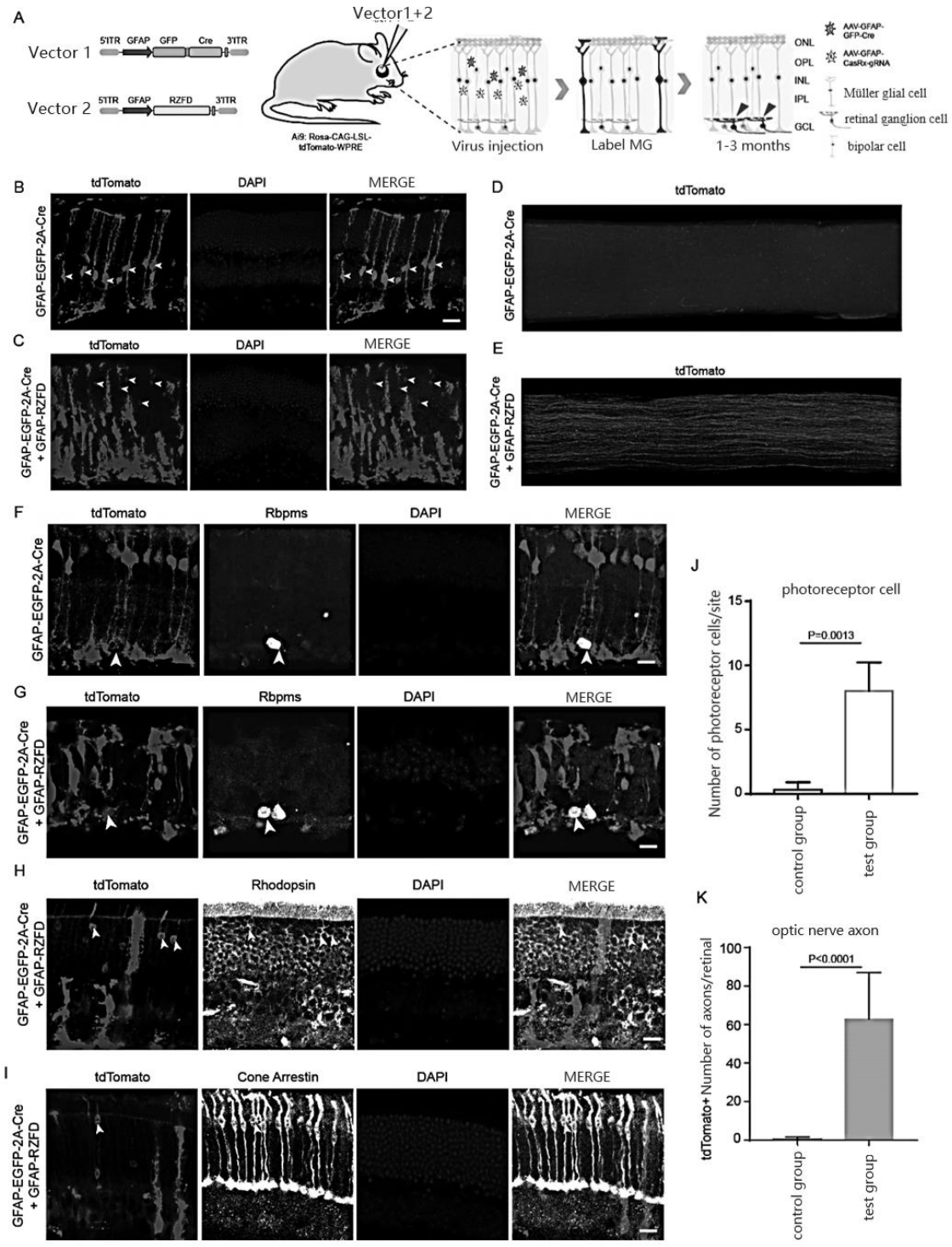

A
Vector 1
5ITR GFAP GFP Cre 3ITR
Vector 2
5ITR GFAP RZFD 3ITR
Vector1+2
Ai9: Rosa-CAG-LSL-tdTomato-WPRE
Virus injection
Label MG
1-3 months
ONL
OPL
INL
IPL
GCL
AAV-GFAP-GFP-Cre
AAV-GFAP-CasRx-gRNA
Müller glial cell
retinal ganglion cell
bipolar cell
B
C
D
E
tdTomato
DAPI
MERGE
GFAP-EGFP-2A-Cre
GFAP-EGFP-2A-Cre + GFAP-RZFD
F
G
H
I
Rbpms
Rhodopsin
Cone Arrestin
J
photoreceptor cell
Number of photoreceptor cells/site
P=0.0013
control group
test group
K
optic nerve axon
tdTomato+ Number of axons/retinal
P<0.0001

Fig. 5

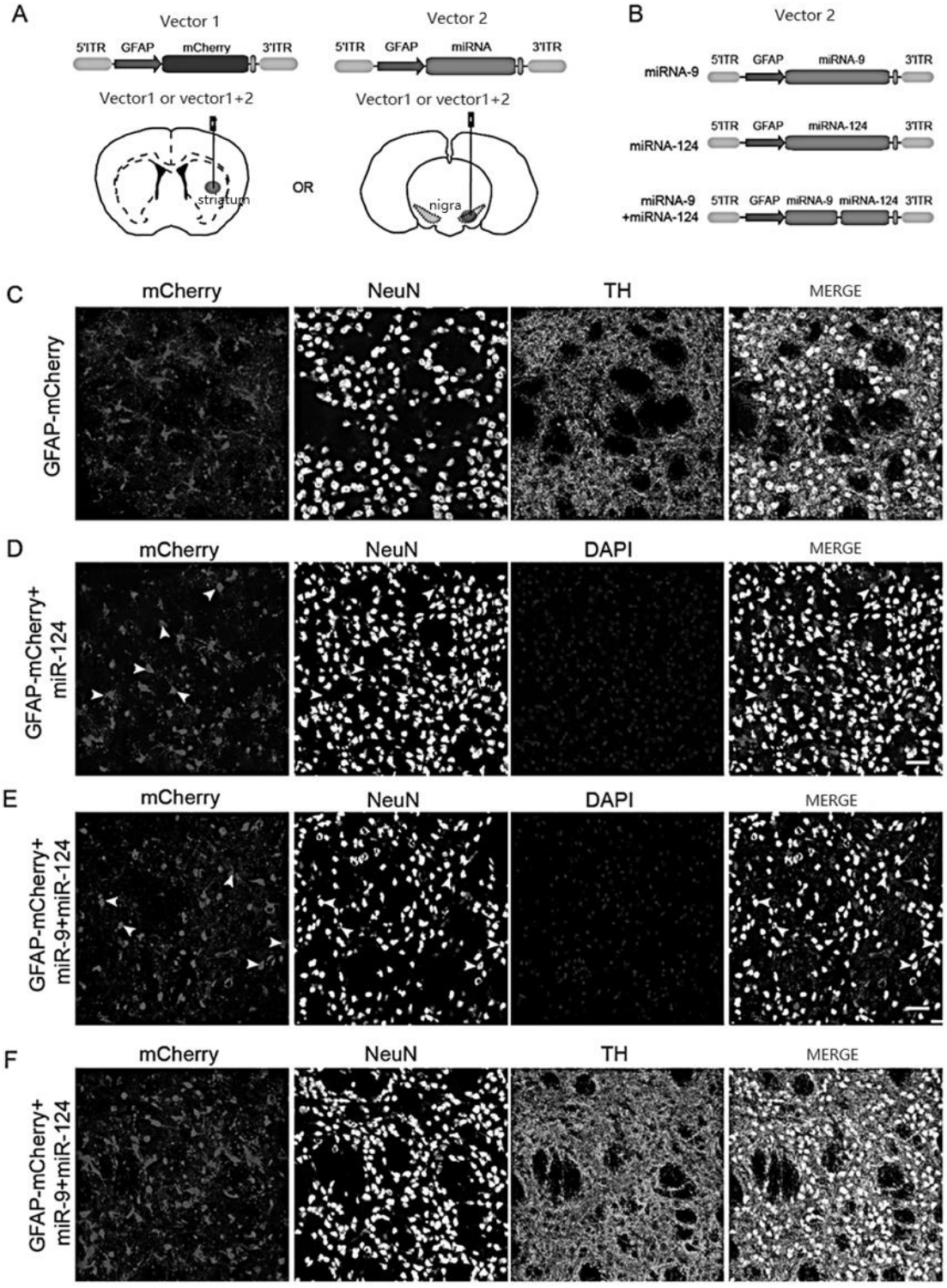

A
Vector 1
5'ITR GFAP mCherry 3'ITR
Vector1 or vector1+2
striatum
OR
Vector 2
5'ITR GFAP miRNA 3'ITR
Vector1 or vector1+2
nigra
B
Vector 2
miRNA-9
5'ITR GFAP miRNA-9 3'ITR
miRNA-124
5'ITR GFAP miRNA-124 3'ITR
miRNA-9 +miRNA-124
5'ITR GFAP miRNA-9 miRNA-124 3'ITR
C
mCherry
NeuN
TH
MERGE
GFAP-mCherry
D
mCherry
NeuN
DAPI
MERGE
GFAP-mCherry+ miR-124
E
mCherry
NeuN
DAPI
MERGE
GFAP-mCherry+ miR-9+miR-124
F
mCherry
NeuN
TH
MERGE
GFAP-mCherry+ miR-9+miR-124

Fig. 6

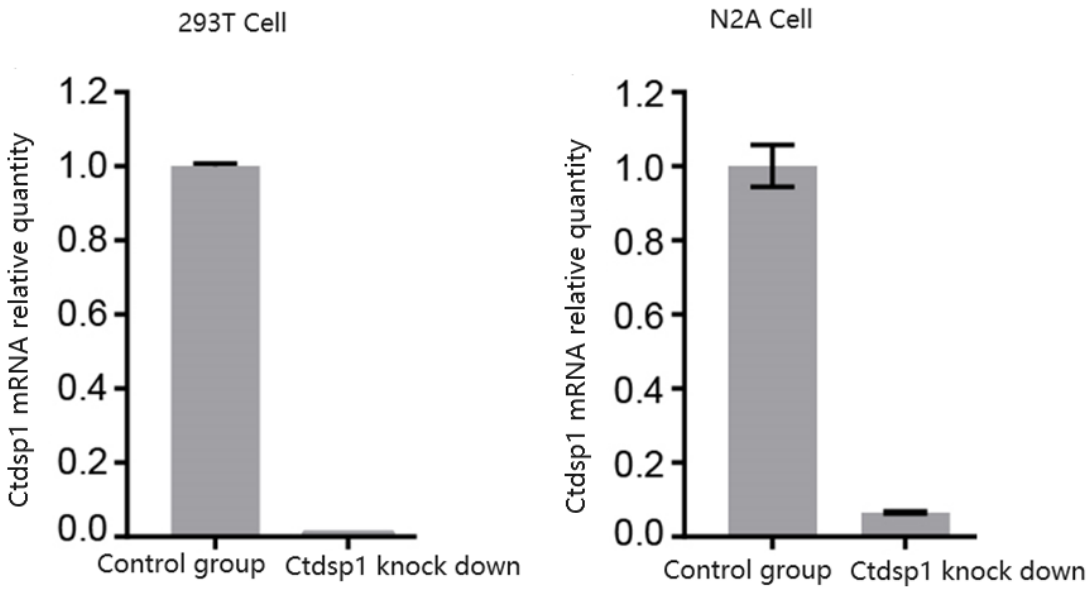

293T Cell
Ctdsp1 mRNA relative quantity
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Control group
Ctdsp1 knock down
N2A Cell
Ctdsp1 mRNA relative quantity
1.2
1.0
0.8
0.6
0.4
0.2
0.0
Control group
Ctdsp1 knock down

Fig. 7

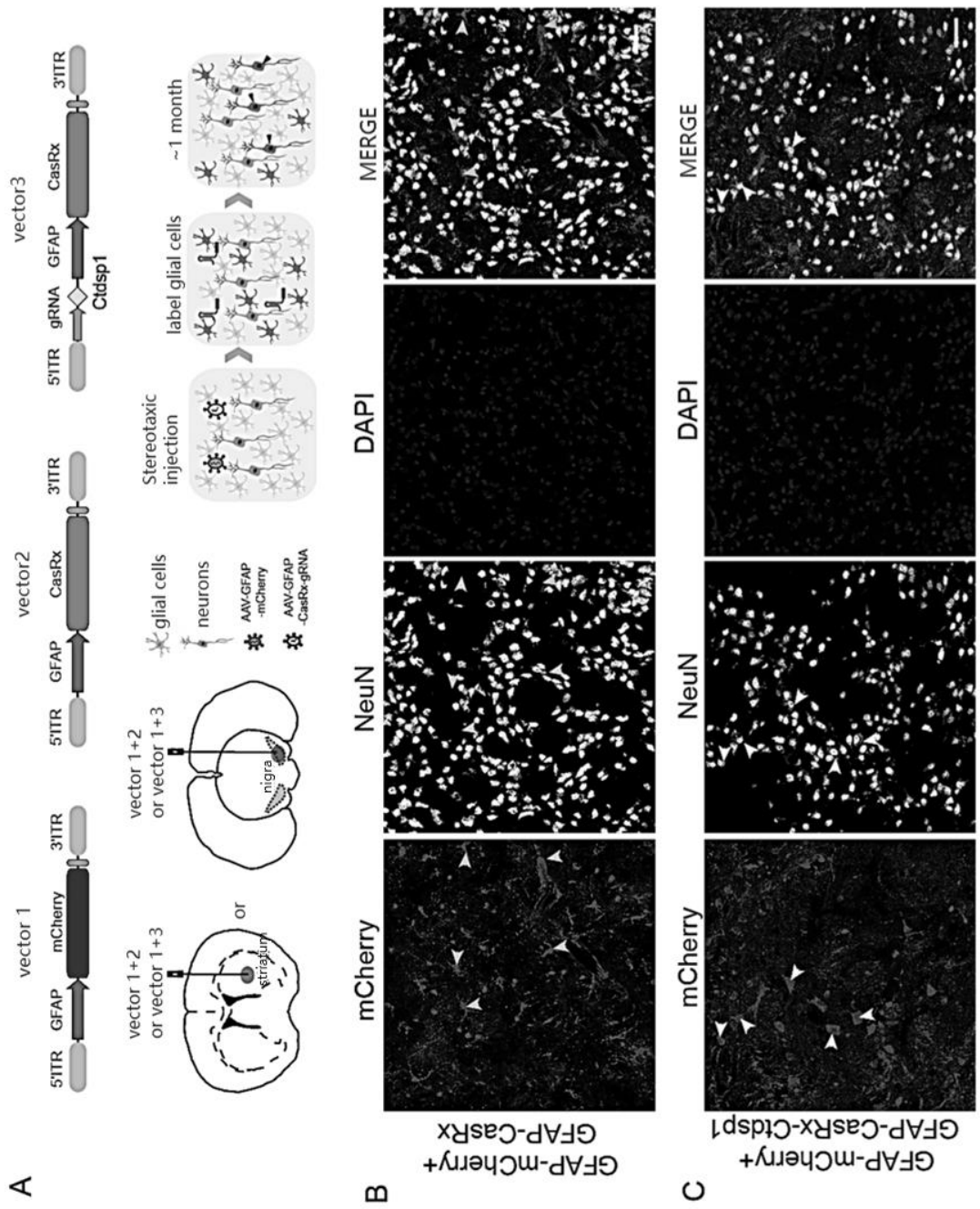

A
vector 1
5'ITR
GFAP
mCherry
3'ITR
vector2
5'ITR
GFAP
CasRx
3'ITR
vector3
5'ITR
gRNA
GFAP
CasRx
3'ITR
Ctdsp1
vector 1+2
or vector 1+3
or
striatum
vector 1+2
or vector 1+3
nigra
glial cells
neurons
AAV-GFAP
-mCherry
AAV-GFAP
-CasRx-gRNA
Stereotaxic
injection
label glial cells
~1 month
B
mCherry
NeuN
DAPI
MERGE
GFAP-mCherry+
GFAP-CasRX
C
mCherry
NeuN
DAPI
MERGE
GFAP-mCherry+
GFAP-CasRx-Ctdsp1

Fig. 8

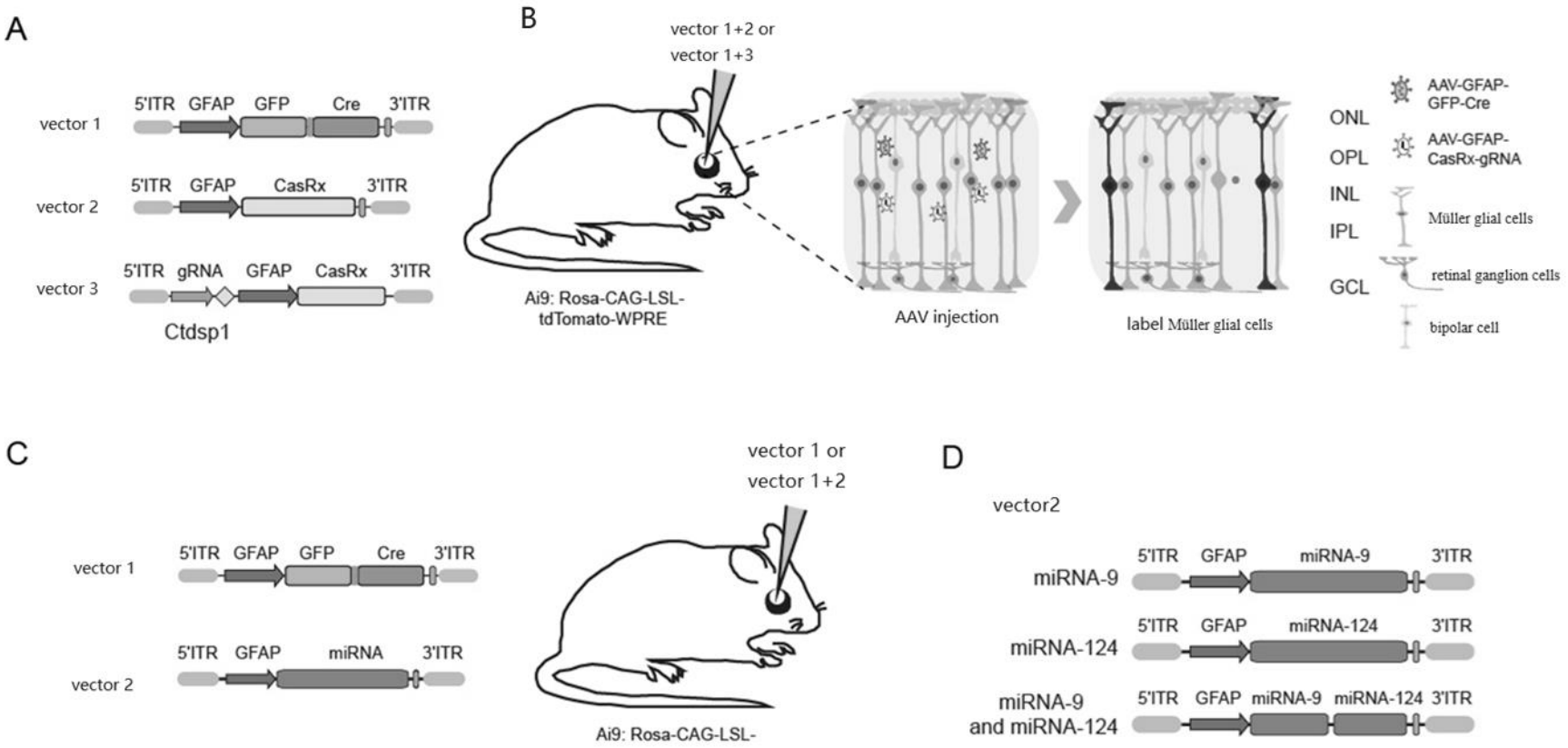

A
vector 1
5'ITR GFAP GFP Cre 3'ITR
vector 2
5'ITR GFAP CasRx 3'ITR
vector 3
5'ITR gRNA GFAP CasRx 3'ITR
Ctdsp1
B
vector 1+2 or
vector 1+3
Ai9: Rosa-CAG-LSL-
tdTomato-WPRE
AAV injection
label Müller glial cells
ONL
OPL
INL
IPL
GCL
AAV-GFAP-
GFP-Cre
AAV-GFAP-
CasRx-gRNA
Müller glial cells
retinal ganglion cells
bipolar cell
C
vector 1 or
vector 1+2
vector 1
5'ITR GFAP GFP Cre 3'ITR
vector 2
5'ITR GFAP miRNA 3'ITR
Ai9: Rosa-CAG-LSL-
D
vector2
miRNA-9
5'ITR GFAP miRNA-9 3'ITR
miRNA-124
5'ITR GFAP miRNA-124 3'ITR
miRNA-9
and miRNA-124
5'ITR GFAP miRNA-9 miRNA-124 3'ITR

Fig. 9