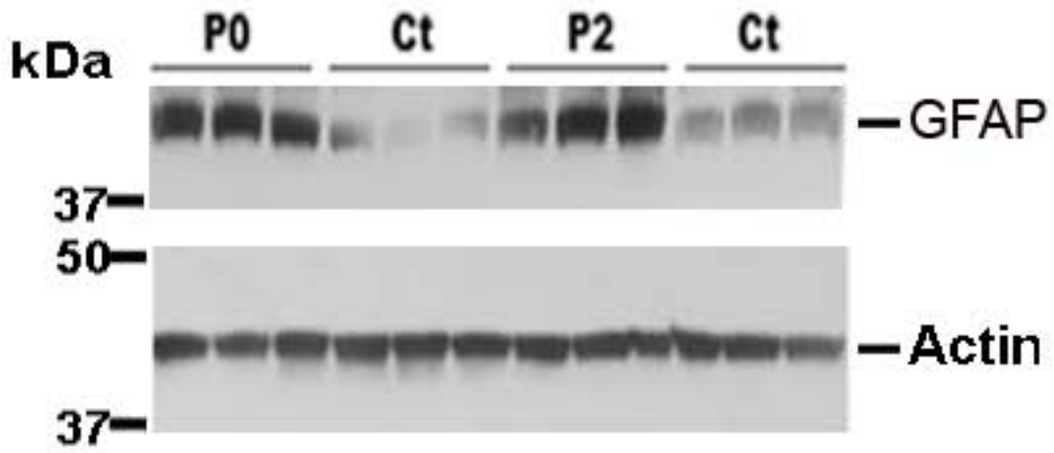
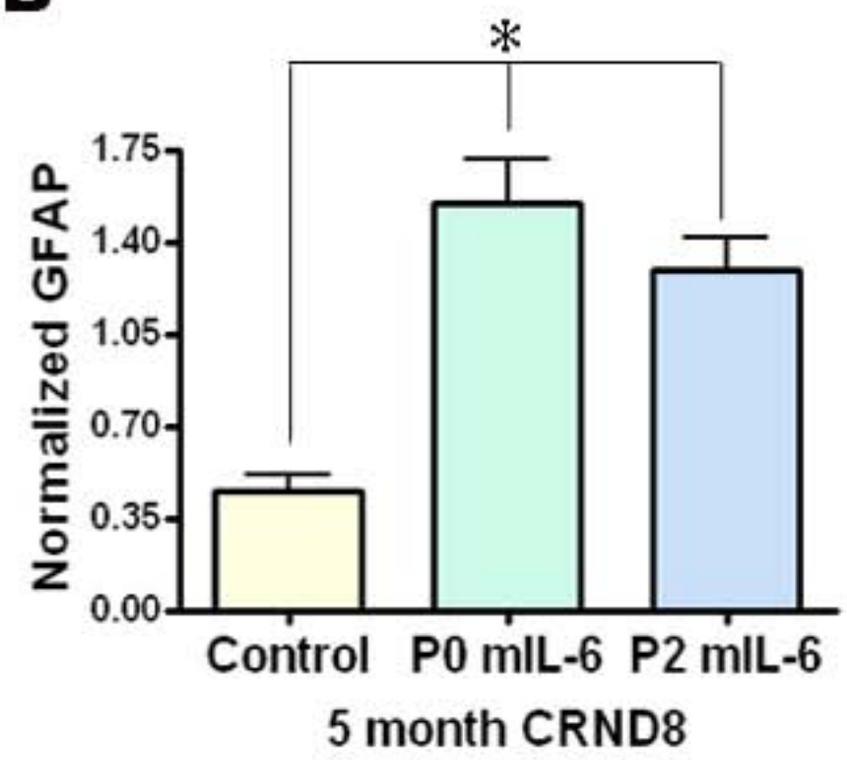
A



B

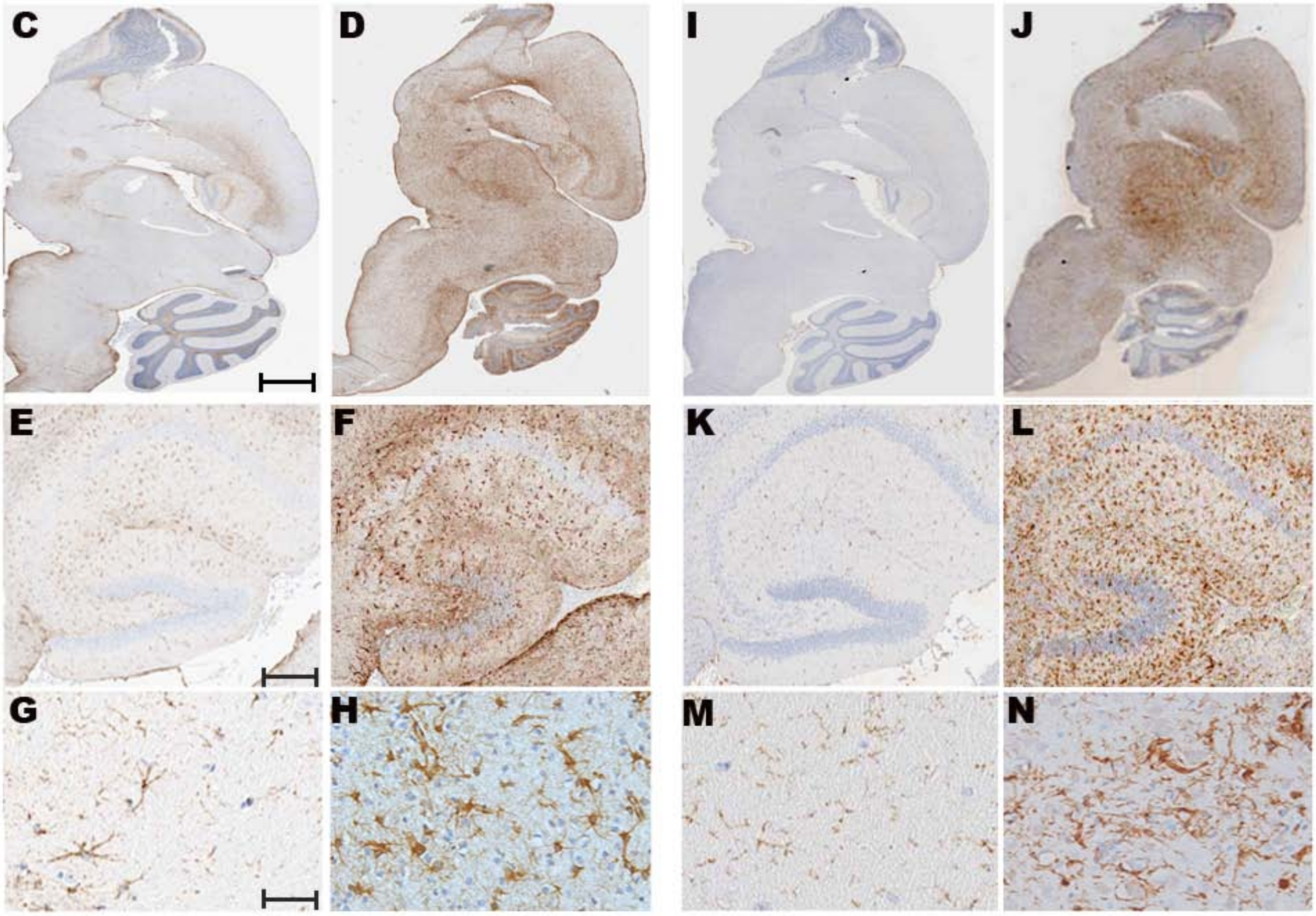


GFAP

Iba-1

NonTg-Control NonTg-mIL6

NonTg-Control NonTg-mIL6



Suppl. Fig.1

GFAP

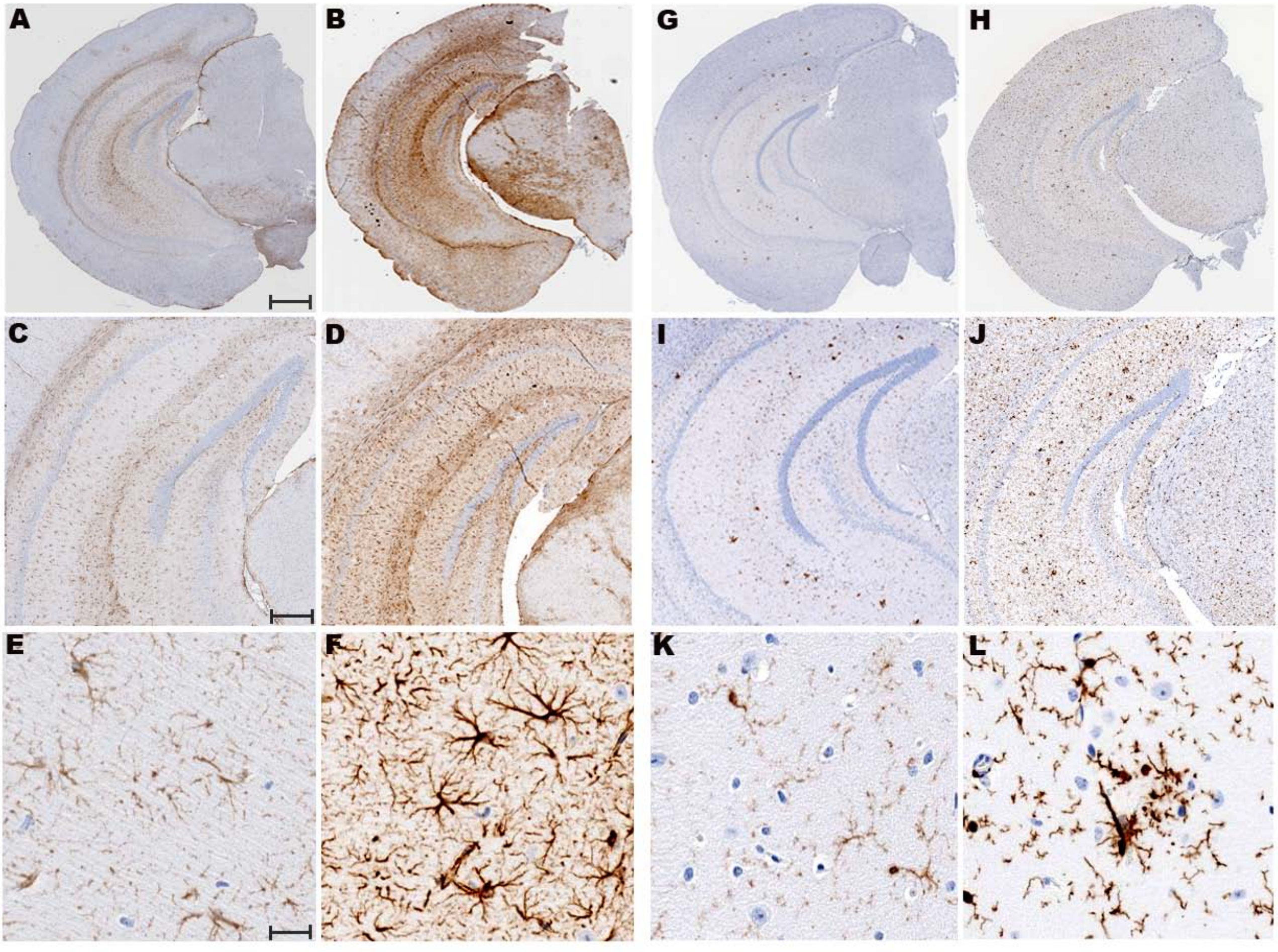
Iba-1

Tg-Control

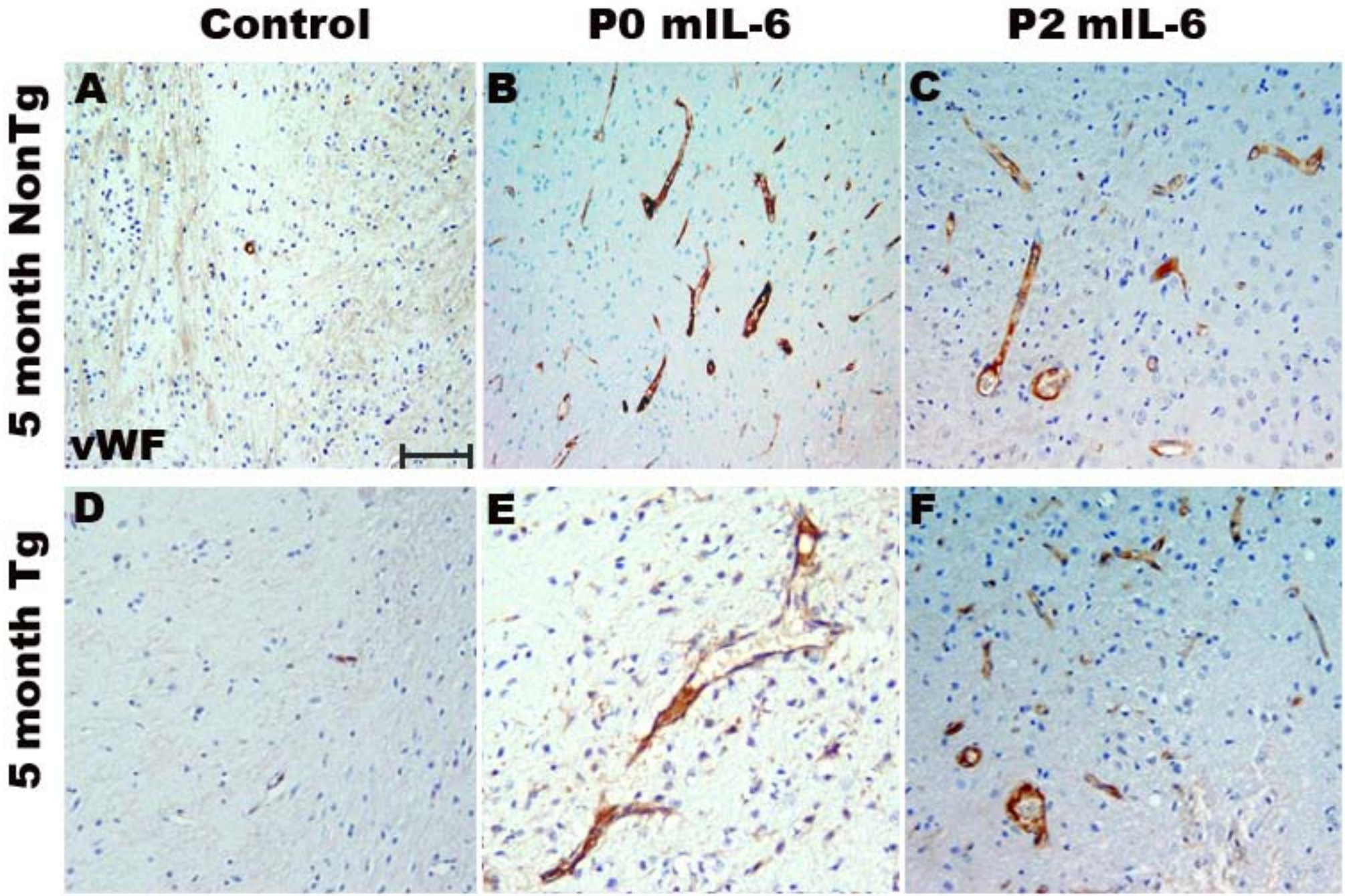
Tg-mIL-6

Tg-Control

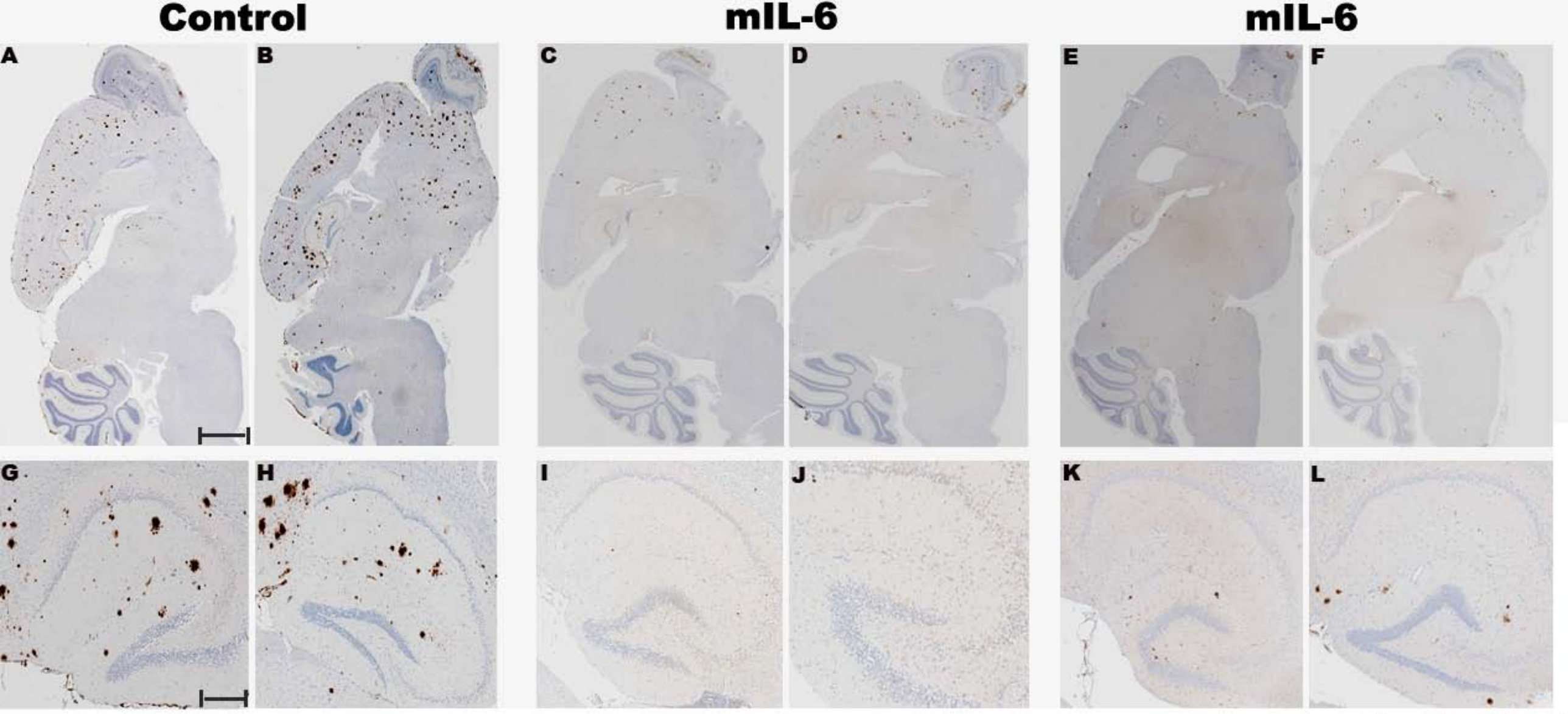
Tg-mIL-6



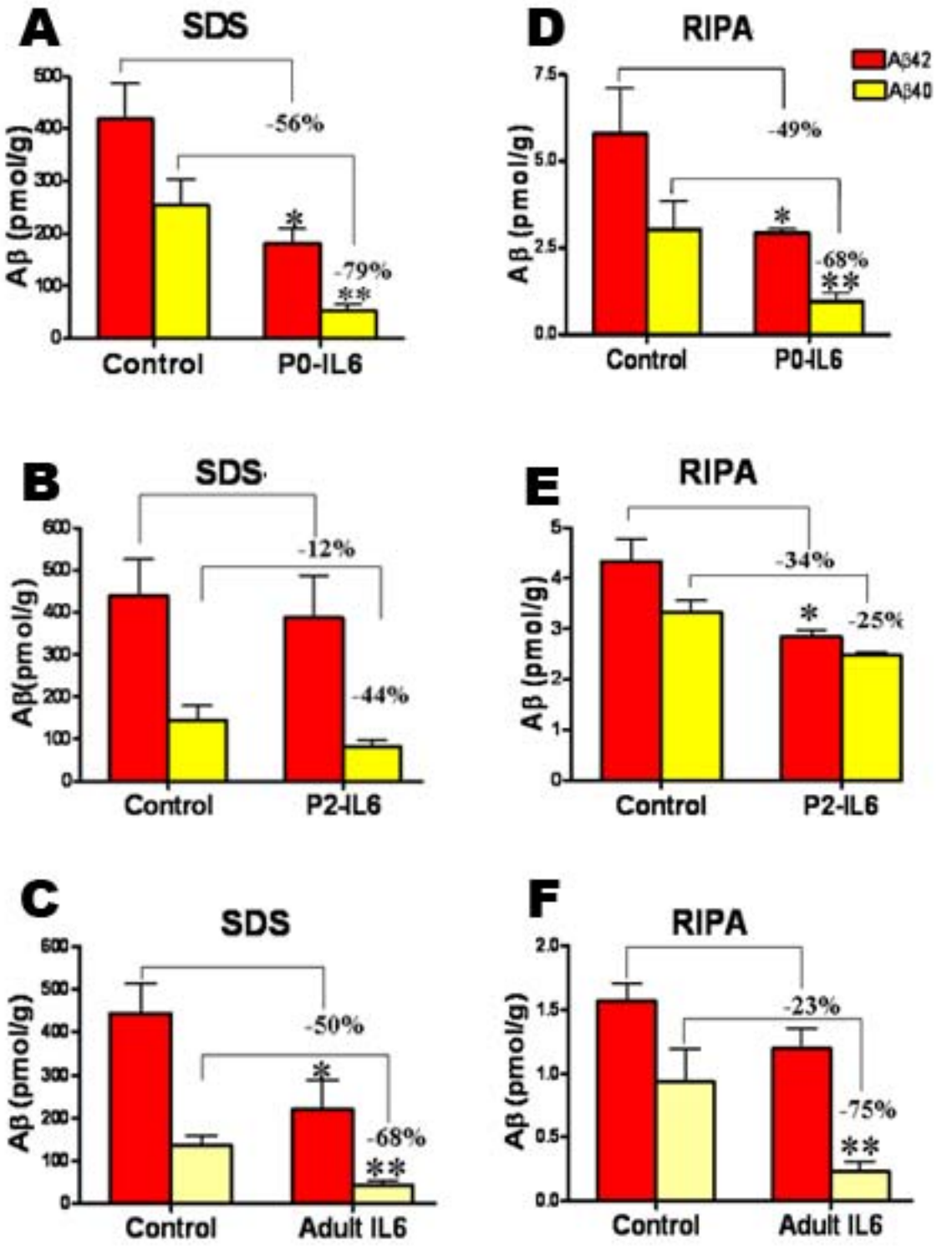
Suppl. Fig. 2



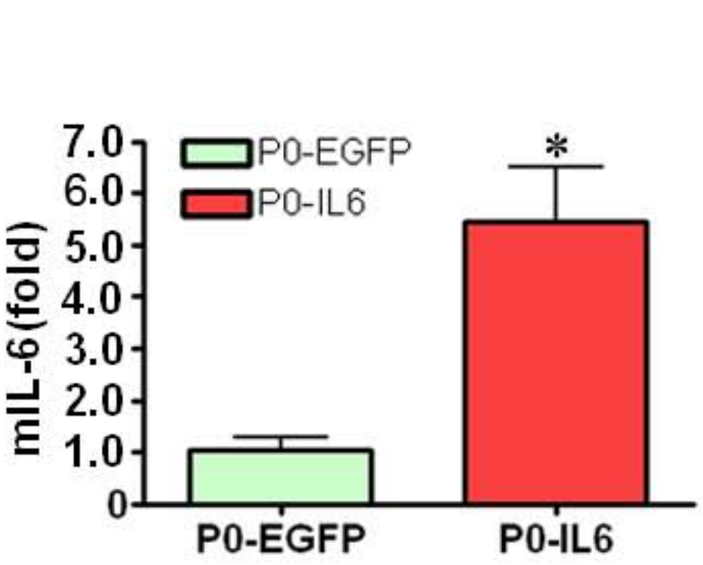
Suppl. Fig. 3

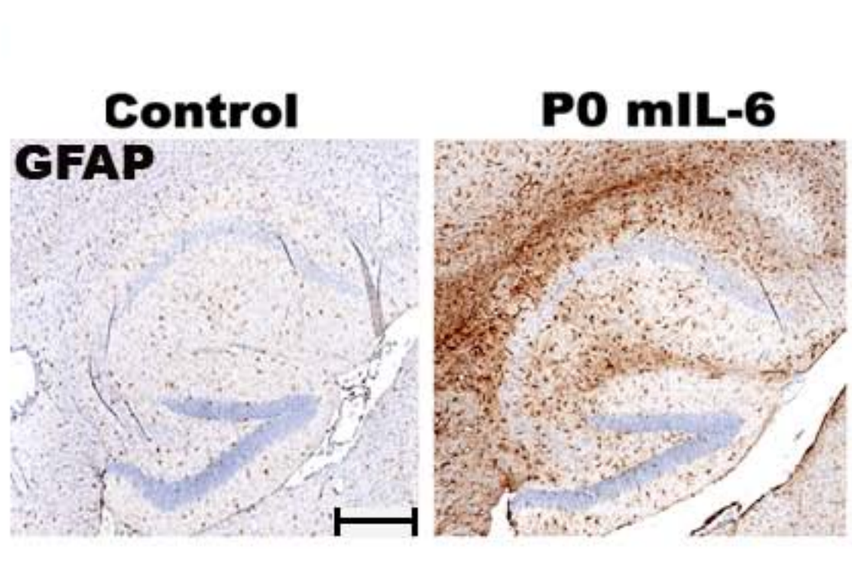


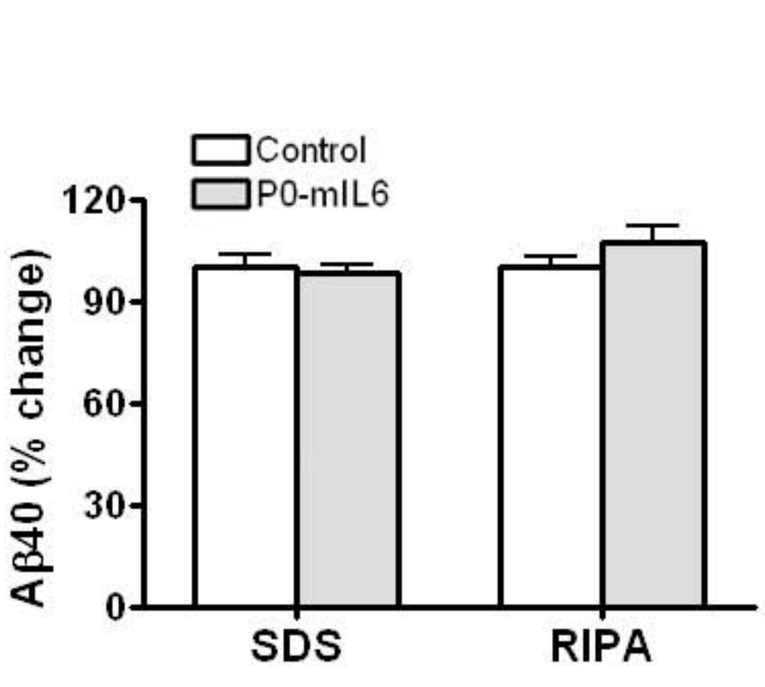
Suppl. Fig. 4

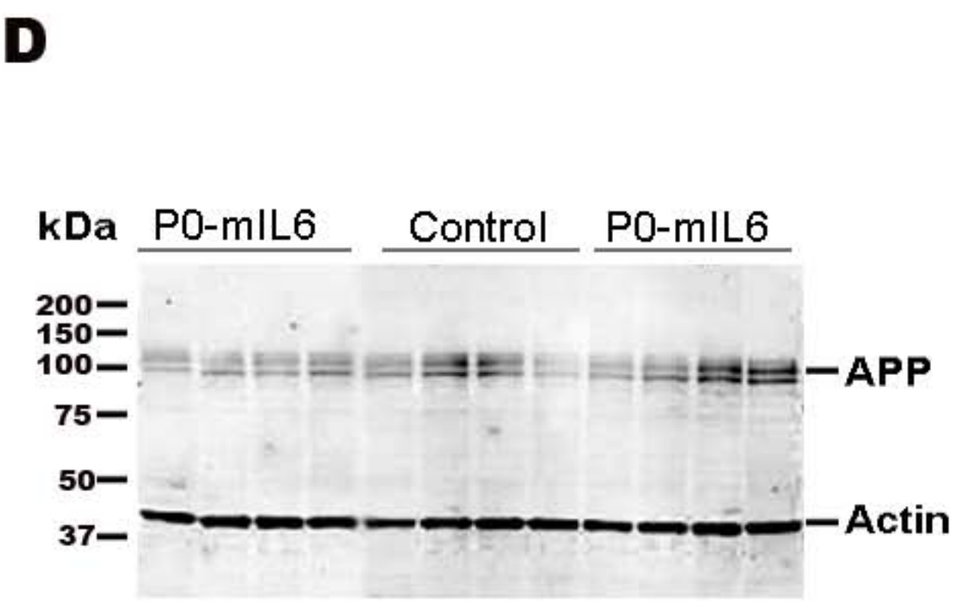

A
SDS
Aβ (pmol/g)
500
400
300
200
100
0
-56%
-79%
*
**
Control
P0-IL6
D
RIPA
Aβ42
Aβ40
7.5
5.0
2.5
0.0
-49%
-68%
*
**
Control
P0-IL6
B
SDS
Aβ(pmol/g)
600
500
400
300
200
100
0
-12%
-44%
Control
P2-IL6
E
RIPA
Aβ (pmol/g)
5
4
3
2
1
0
-34%
-25%
*
Control
P2-IL6
C
SDS
Aβ (pmol/g)
600
500
400
300
200
100
0
-50%
-68%
*
**
Control
Adult IL6
F
RIPA
Aβ (pmol/g)
2.0
1.5
1.0
0.5
0.0
-23%
-75%
**
Control
Adult IL6

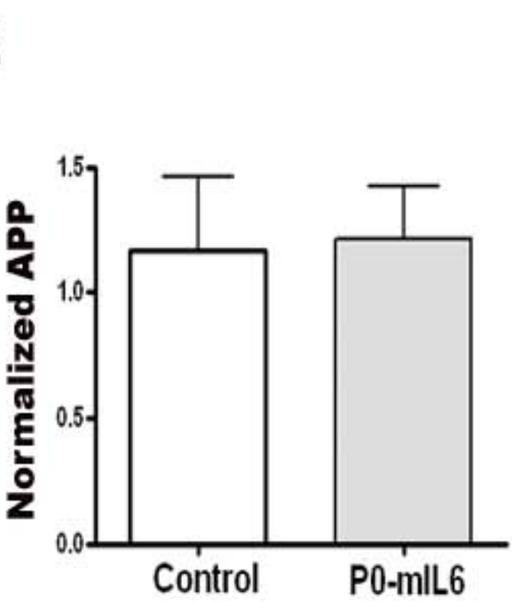
Suppl. Fig.5


A
mIL-6(fold)
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
P0-EGFP
P0-IL6
*
P0-EGFP
P0-IL6


B
Control
P0 mIL-6
GFAP


C
Control
P0-mIL6
Aβ40 (% change)
120
90
60
30
0
SDS
RIPA


D
kDa
P0-mIL6
Control
P0-mIL6
200
150
100
75
50
37
APP
Actin


E
Normalized APP
1.5
1.0
0.5
0.0
Control
P0-mIL6

Suppl. Fig 6

SUPPLEMENTARY MATERIALS

Supplementary Figure Legends

Suppl. Fig 1. Gliosis profile in mIL-6 injected P0→5mo CRND8 mice.

A-B. Representative immunoblot of GFAP levels in P0→5mo and P2→5mo mIL-6 injected TgCRND8 mice compared to controls ("Ct") (A). Intensity analysis of GFAP immunoreactive bands normalized to β actin is depicted (B) (**p*<0.05).

C-N. Upregulation of GFAP positive astrocytes as well as Iba-1 positive microglia in P0→5mo mIL-6 injected non-transgenic CRND8 littermates ("NonTg-mIL6") compared to age-matched controls ("NonTg-Control"). The top panels (C, D, I, J) show the whole brain sections whereas the bottom panels (E-H, K-N) show higher magnifications of the corresponding hippocampus. *Scale Bar,* 600μm (C, D, I, J), 150 μm (E, F, K, L) and 25 μm (G, H, M, N).

Suppl. Fig 2. AAV1-mIL-6 expression following stereotaxic injection in the hippocampus of young adult TgCRND8 mice results in reactive astrogliosis and microgliosis.

AAV1-mIL-6 or AAV1-EGFP was injected into the hippocampus of 4 month old TgCRND8 mice and brain sections analyzed after 6 weeks. Whole brain panels showing a coronal section in the immediate vicinity of AAV1 injection site was stained with anti-GFAP **(A-F)** or anti-Iba-1 **(G-L)** antibodies. Whole brain sections on top and

higher magnification panels below highlight the activated glial morphology in the hippocampus of mIL-6 expressing mice ("Tg-mIL6") compared to EGFP expressing mice ("Tg-Control"). *Scale Bar,* 600μm (A, B, G, H), 150μm (C, D, I, J) and 25μm (E, F, K, L).

Suppl. Fig 3. Proliferative angiopathy in P0→5mo mIL-6 expressing CRND8 mice.

Representative micrographs of 5 month old non-transgenic littermates (B, C) and transgenic TgCRND8 mice (E, F) injected with AAV1-mIL-6 on day P0 (B, E) or day P2 (C, F) showing extensive proliferative angiopathy compared with age matched control mice (A, nontransgenic control and D, transgenic control). *Scale Bar,* 25 μm.

Suppl. Fig 4. Significant attenuation of Aβ deposition in P0→5mo and P2→5mo AAV1-mIL-6 expressing TgCRND8 mice.

TgCRND8 mice injected with AAV1-mIL-6 or AAV1-EGFP on neonatal day P0 (E-L) or P2 (C-J) and then analyzed at 5 months. Representative whole brain sections (A-F) and corresponding hippocampus (G-L) stained with 33.1.1 antibody (pan Aβ1-16) of 2 mice from each paradigm is shown. *Scale Bar,* 600μm (A-F), 150 μm (G-L).

Suppl. Fig. 5. Attenuation in RIPA and SDS extractable Aβ levels in mIL-6 injected mice.

Biochemical analyses of SDS and RIPA extractable Aβ42 and Aβ40 levels in P0→5mo mIL-6 expressing TgCRND8 mice (A, D), P2→5mo mIL-6 expressing CRND8 mice (B, E), and 4→5.5mo mIL-6 expressing TgCRND8 (C, F) compared to EGFP expressing age matched controls (**p*<0.05 and ***p*<0.05).

Suppl. Fig 6. No evidence of changes in steady state Aβ production or APP levels in mIL-6 injected P0→3mo Tg2576 mice.

A. P0 AAV1-mIL-6 injected 3 month old Tg2576 mice show increased levels of mIL-6 in the RIPA soluble brain extracts compared to age-matched control mice (*n*=6-9/group). **p*<0.05

B. Increased GFAP immunoreactive astrocytes is evident in paraffin embedded brain sections of P0→3mo mIL-6 injected Tg2576 mice compared to controls. *Scale Bar,* 150μm

C. Steady state levels of Aβ40 is not significantly altered in mIL-6 expressing Tg2576 mice at 3 months (*n*=6-9/group) as measured by ELISA using RIPA soluble brain extracts.

D-E. Representative anti CT20 immunoblot showing no significant changes in APP levels in 3 month old Tg2576 mice injected with AAV1-mIL-6 on day P0 compared to age-matched controls (D). Quantitative analysis of anti CT20 immunoreactive APP levels was normalized to β actin in P0→3mo Tg2576 mice (E).

Supplementary Table 1: Summary of changes in Aβ levels following rAAV1 mediated overexpression of mIL-6 in mice brain.

Mouse	mIL6 (fold over control)	Injection	Length of treatment	FA Aβ42 (% over control)	FA Aβ40 (% over control)	Forebrain plaque burden (% change)
TgCRND8	7.81 ∗	P0	5 mo	-60 ∗	-89 ∗	-67 ∗
TgCRND8	3.42 ∗	P2	5 mo	-56 ∗	-62 ∗	-50 ∗
TgCRND8	2.0	4 mo adult	1.5 mo	-47	-73 ∗	-60 ∗
Tg2576	5.5∗	P0	3 mo	-	-1.6 (SDS Aβ40)	-

∗p<0.05