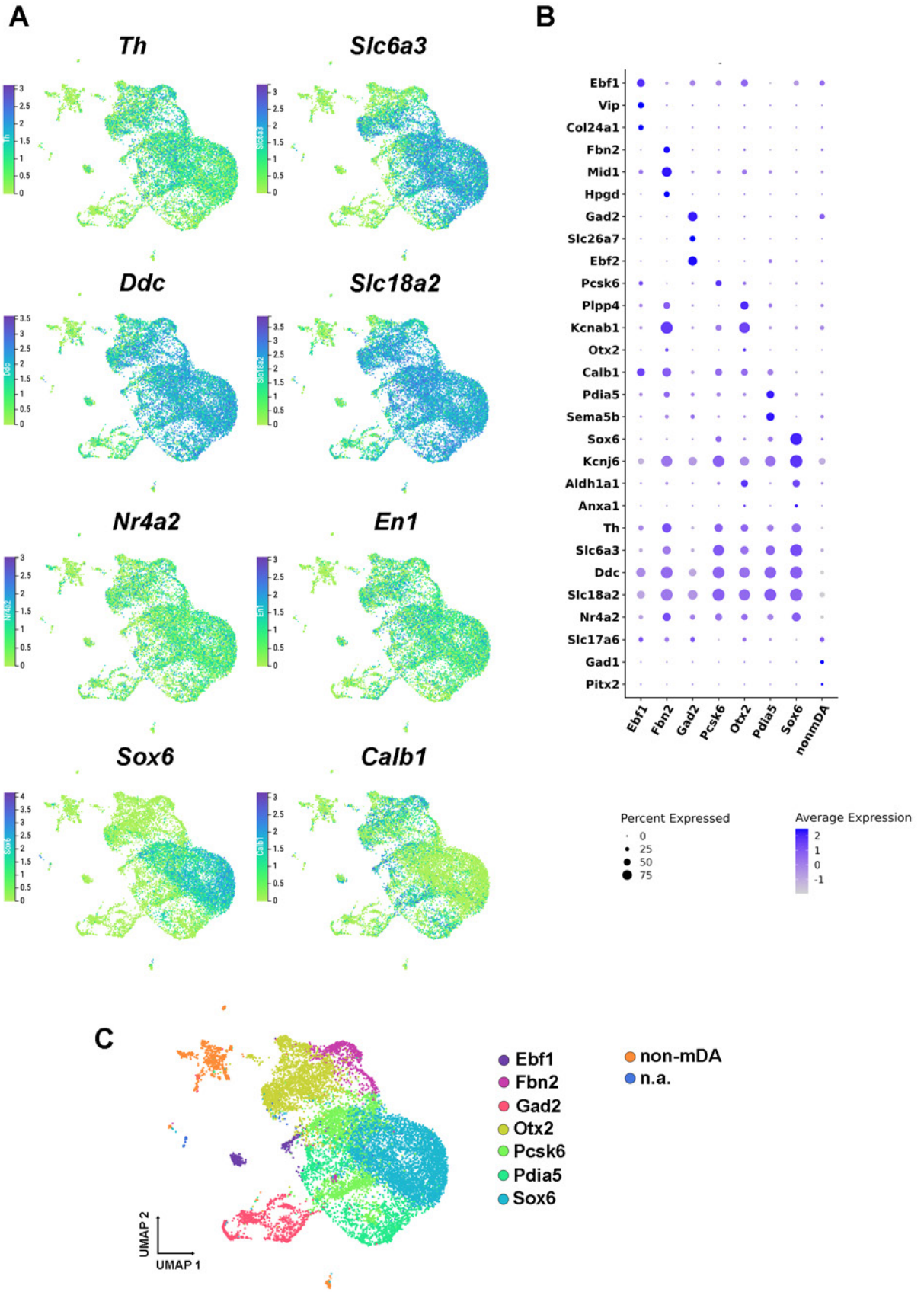
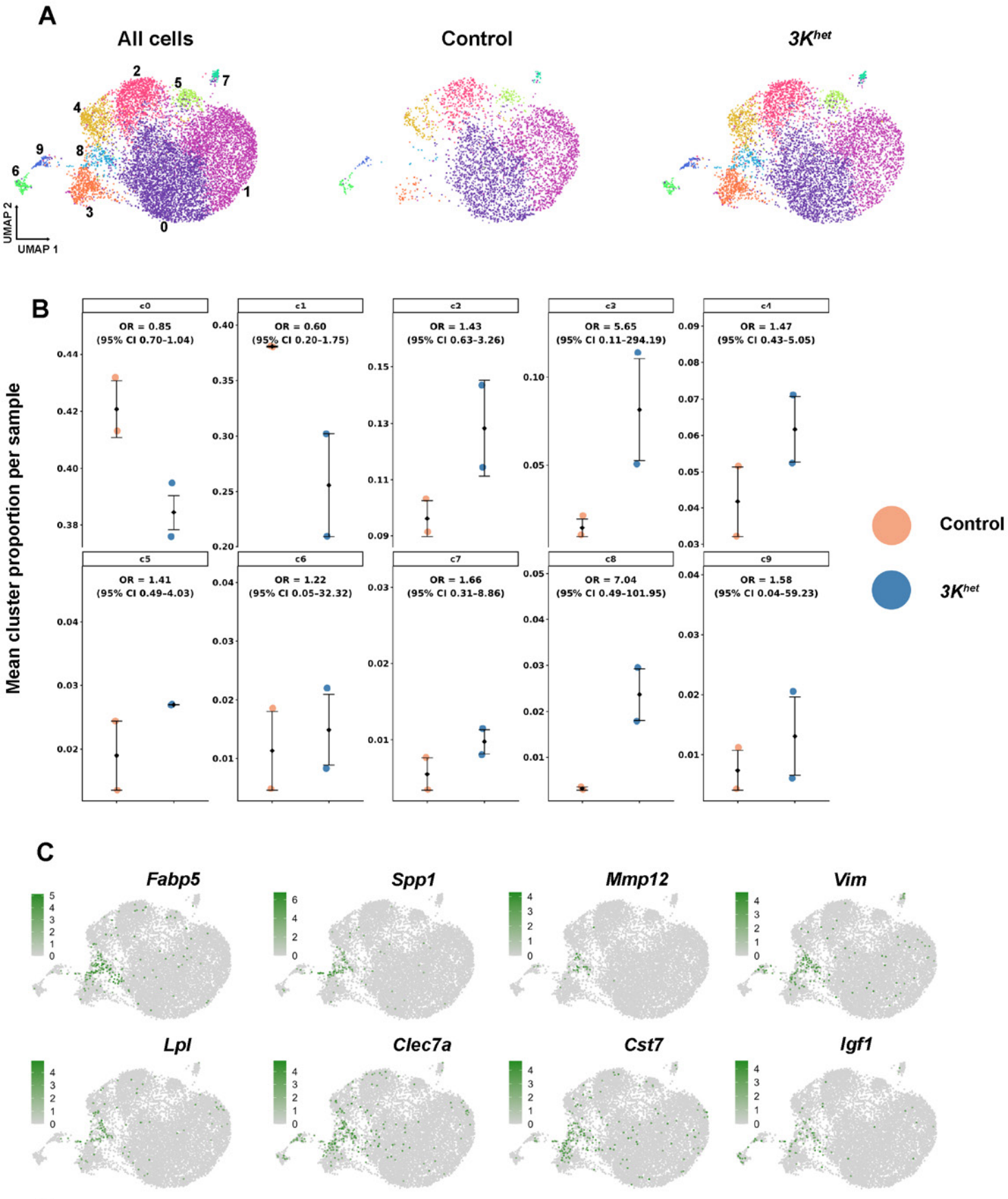
Suppl.Fig 1


A
Th
Slc6a3
Ddc
Slc18a2
Nr4a2
En1
Sox6
Calb1
B
Ebf1
Vip
Col24a1
Fbn2
Mid1
Hpgd
Gad2
Slc26a7
Ebf2
Pcsk6
Plpp4
Kcnab1
Otx2
Calb1
Pdia5
Sema5b
Sox6
Kcnj6
Aldh1a1
Anxa1
Th
Slc6a3
Ddc
Slc18a2
Nr4a2
Slc17a6
Gad1
Pitx2
Ebf1
Fbn2
Gad2
Pcsk6
Otx2
Pdia5
Sox6
nonmDA
Percent Expressed
0
25
50
75
Average Expression
2
1
0
-1
C
UMAP 2
UMAP 1
Ebf1
Fbn2
Gad2
Otx2
Pcsk6
Pdia5
Sox6
non-mDA
n.a.

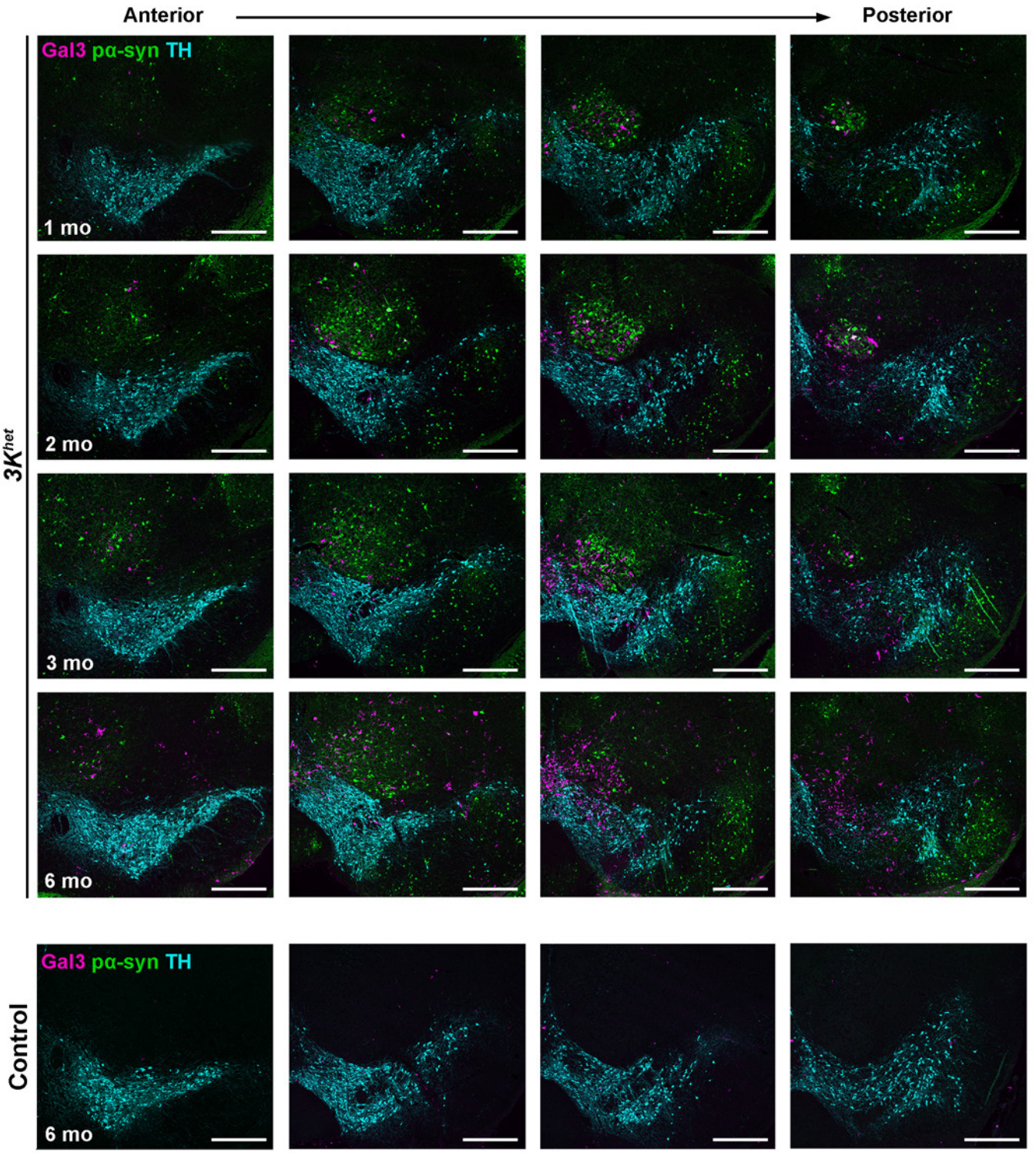
Suppl.Fig 2



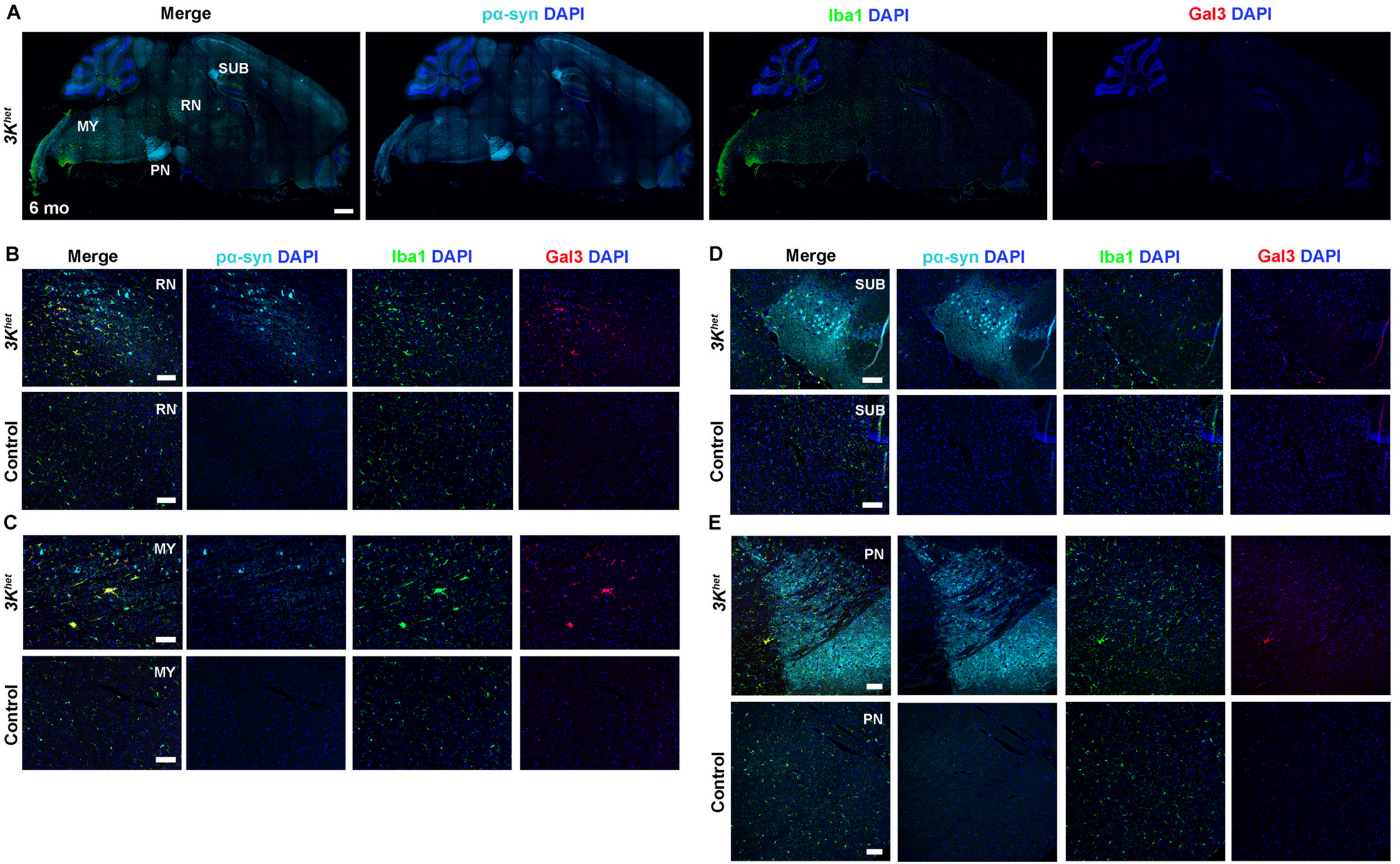
D

GO-term, Biological process, downregulated in 3K het microglia	Overlap	Adj. P-value	Combined score	Genes
Synapse Pruning (GO:0098883)	4/8	3,43405E-05	3573,370725	C1QB; ITGAM; TREM2; C1QC
Microglial Cell Activation (GO:0001774)	3/19	0,044204934	354,8585255	C1QA; ITGAM; TREM2
Cell Junction Disassembly (GO:0150146)	2/5	0,044204934	1139,724512	C1QB; C1QC
Negative Regulation of Membrane Protein Ectodomain Proteolysis (GO:0051045)	2/6	0,044204934	813,4966772	ROCK1; TIMP2
Positive Regulation of Amyloid-Beta Clearance (GO:1900223)	2/6	0,044204934	813,4966772	ROCK1; TREM2
Humoral Immune Response Mediated by Circulating Immunoglobulin (GO:0002455)	2/6	0,044204934	813,4966772	C1QB; C1QC
Regulation of Platelet Activation (GO:0010543)	3/29	0,044204934	187,415325	GP9; FCER1G; SELENOP
Protein Insertion Into ER Membrane (GO:0045048)	3/30	0,044204934	178,1239131	WDR83OS; WNK1; EMC10
Antigen Processing and Presentation of Exogenous Peptide Antigen (GO:0002478)	3/31	0,044204934	169,5757397	FCER1G; CTSS; MPEG1
Antigen Processing and Presentation of Exogenous Peptide Antigen via MHC Class I (GO:0042590)	2/7	0,044204934	623,4237937	FCER1G; MPEG1

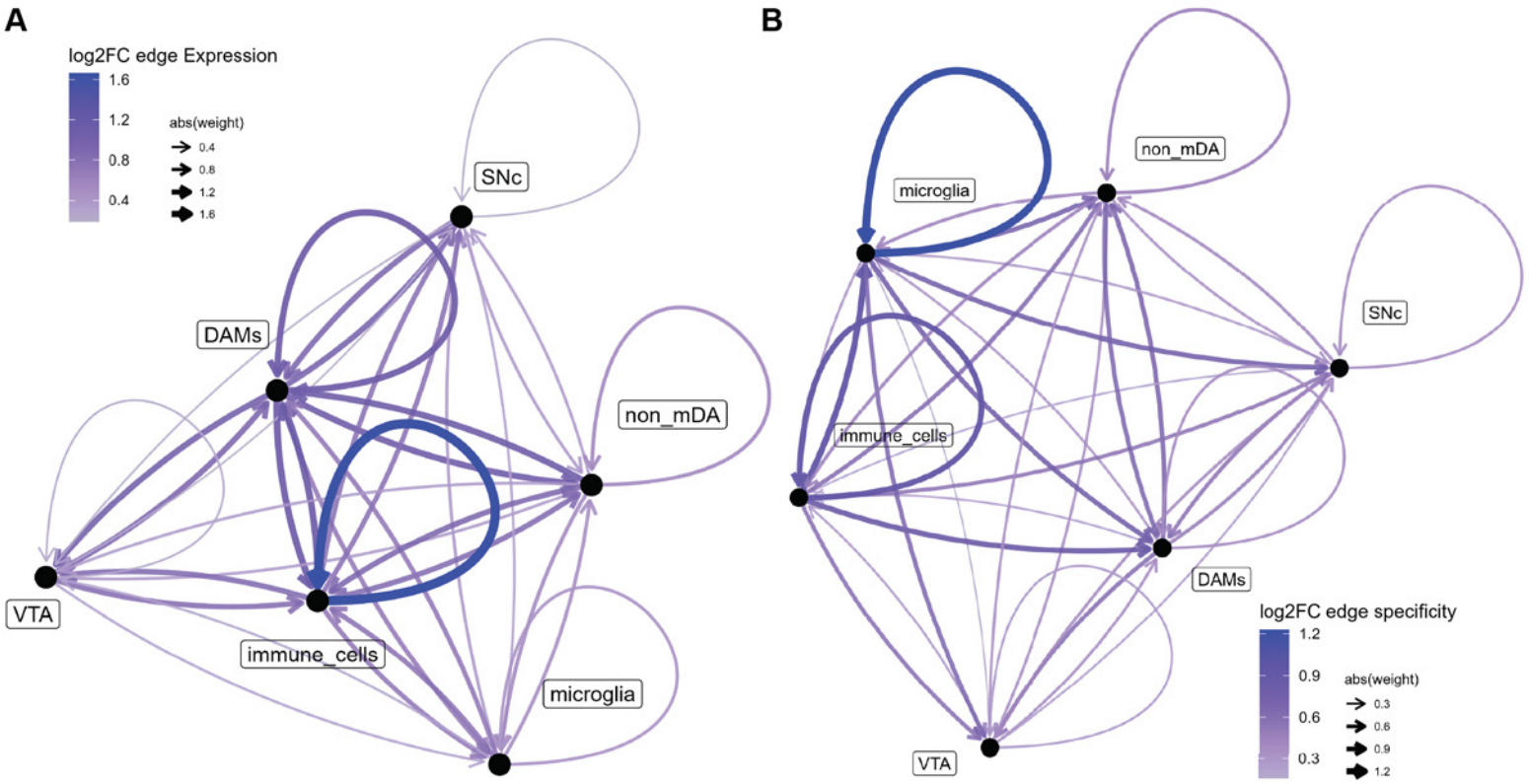
Suppl.Fig 3

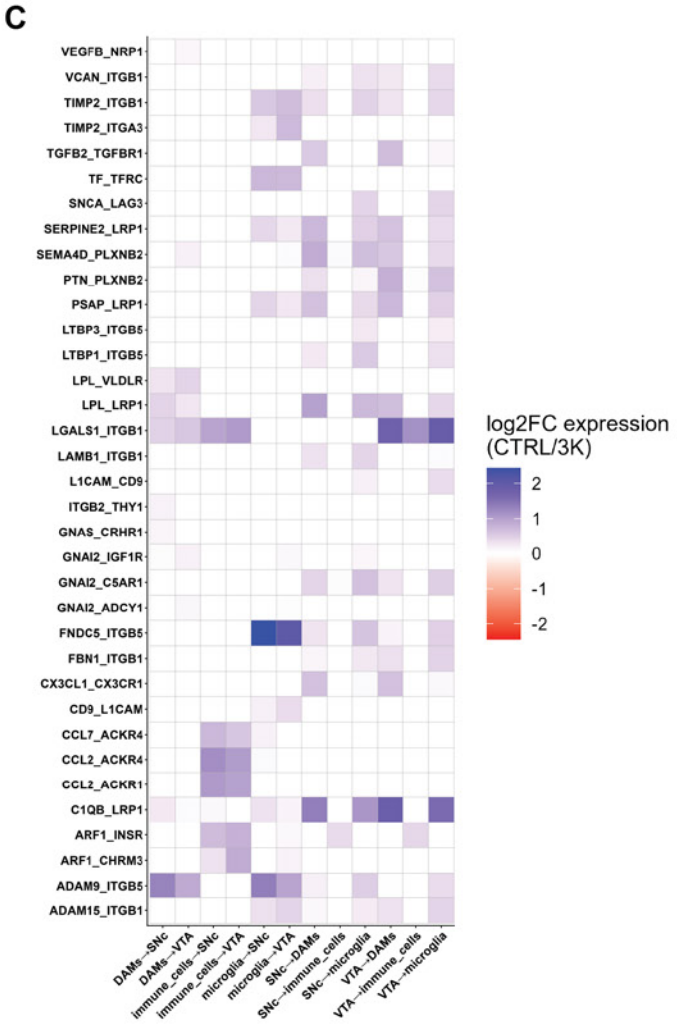

Anterior
Posterior
Gal3 pα-syn TH
1 mo
2 mo
3 mo
6 mo
3K^het
Control
Gal3 pα-syn TH
6 mo

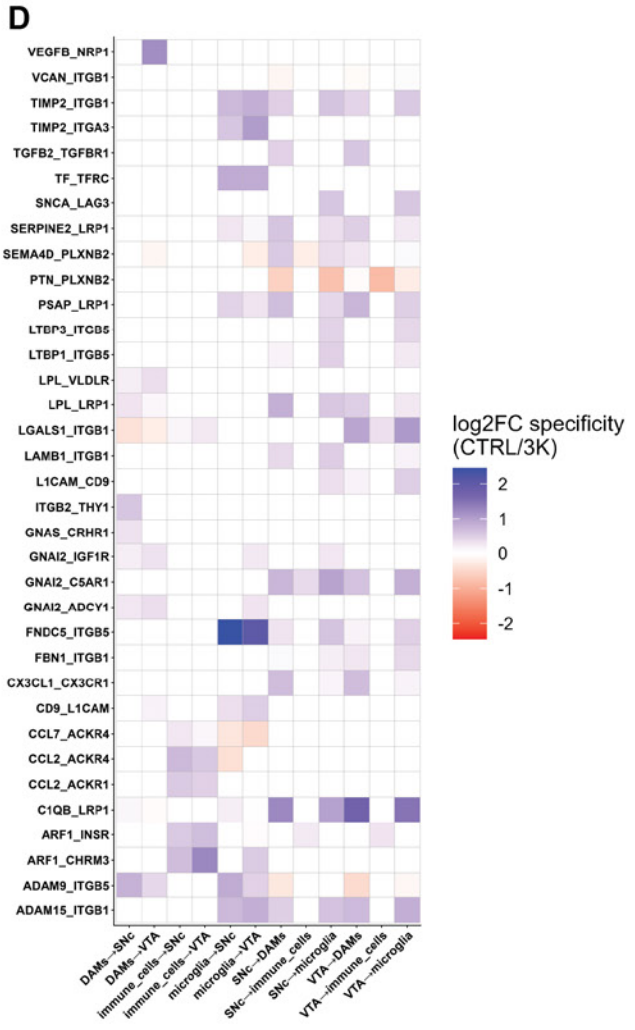
Suppl.Fig 4


A
Merge
pα-syn DAPI
Iba1 DAPI
Gal3 DAPI
3K^het
SUB
RN
MY
PN
6 mo
B
Merge
pα-syn DAPI
Iba1 DAPI
Gal3 DAPI
3K^het
RN
Control
RN
C
3K^het
MY
Control
MY
D
Merge
pα-syn DAPI
Iba1 DAPI
Gal3 DAPI
3K^het
SUB
Control
SUB
E
3K^het
PN
Control
PN

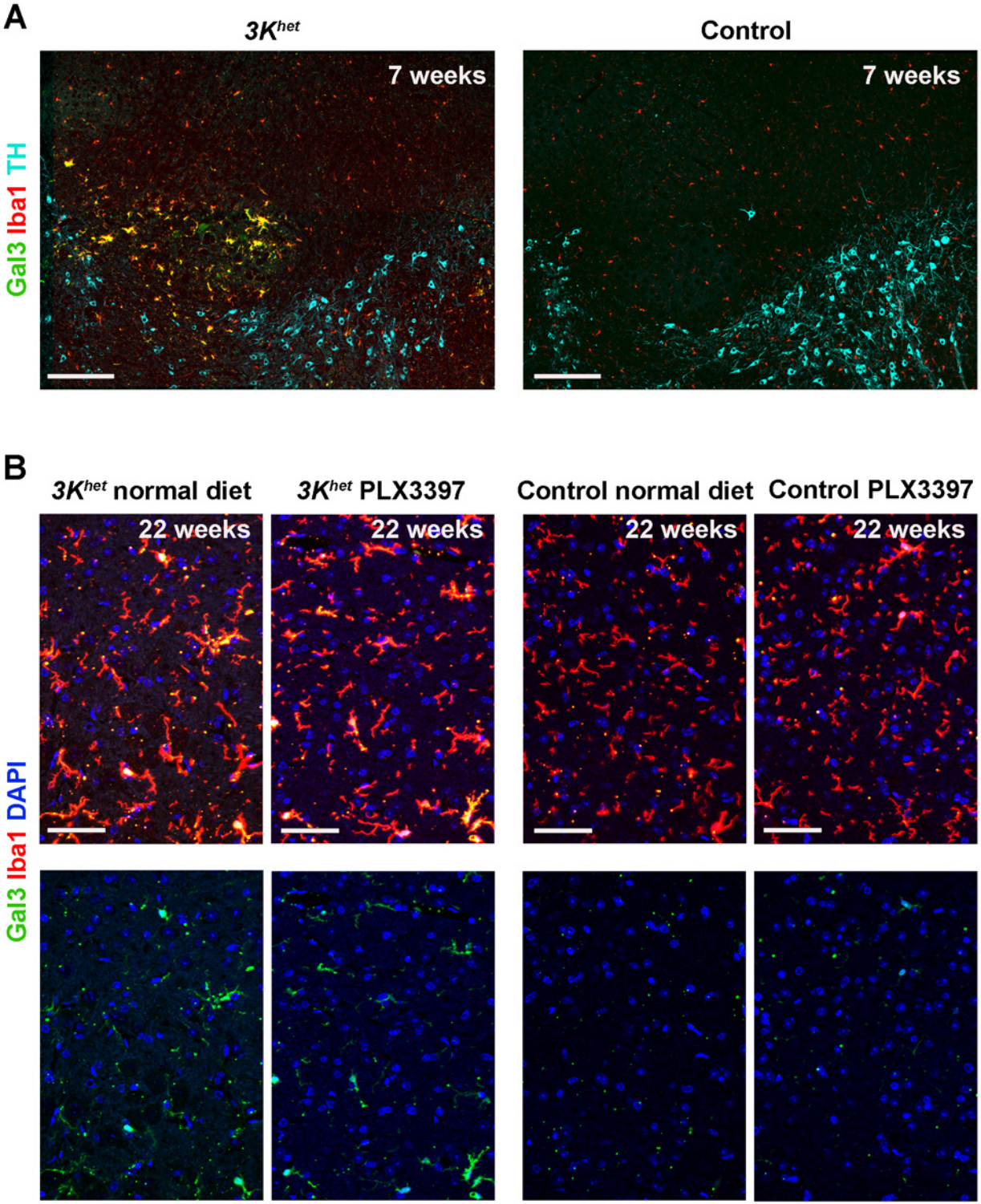
Suppl.Fig 5


A
log2FC edge Expression
1.6
1.2
0.8
0.4
abs(weight)
0.4
0.8
1.2
1.6
SNc
DAMs
non_mDA
VTA
immune_cells
microglia
B
non_mDA
microglia
SNc
immune_cells
DAMs
VTA
log2FC edge specificity
1.2
0.9
0.6
0.3
abs(weight)
0.3
0.6
0.9
1.2

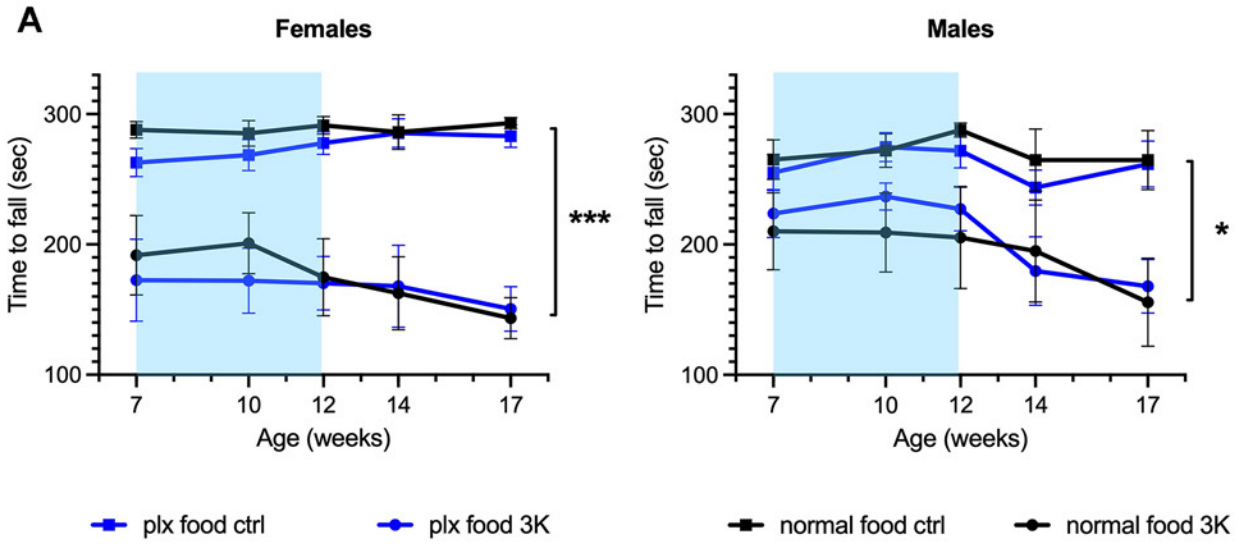

C
VEGFB_NRP1
VCAN_ITGB1
TIMP2_ITGB1
TIMP2_ITGA3
TGFB2_TGFBR1
TF_TFRC
SNCA_LAG3
SERPINE2_LRP1
SEMA4D_PLXNB2
PTN_PLXNB2
PSAP_LRP1
LTBP3_ITGB5
LTBP1_ITGB5
LPL_VLDLR
LPL_LRP1
LGALS1_ITGB1
LAMB1_ITGB1
L1CAM_CD9
ITGB2_THY1
GNAS_CRHR1
GNAI2_IGF1R
GNAI2_C5AR1
GNAI2_ADCY1
FNDC5_ITGB5
FBN1_ITGB1
CX3CL1_CX3CR1
CD9_L1CAM
CCL7_ACKR4
CCL2_ACKR4
CCL2_ACKR1
C1QB_LRP1
ARF1_INSR
ARF1_CHRM3
ADAM9_ITGB5
ADAM15_ITGB1
DAMs→SNc
DAMs→VTA
immune_cells→SNc
immune_cells→VTA
microglia→SNc
microglia→VTA
SNc→DAMs
SNc→immune_cells
SNc→microglia
VTA→DAMs
VTA→immune_cells
VTA→microglia
log2FC expression
(CTRL/3K)
2
1
0
-1
-2

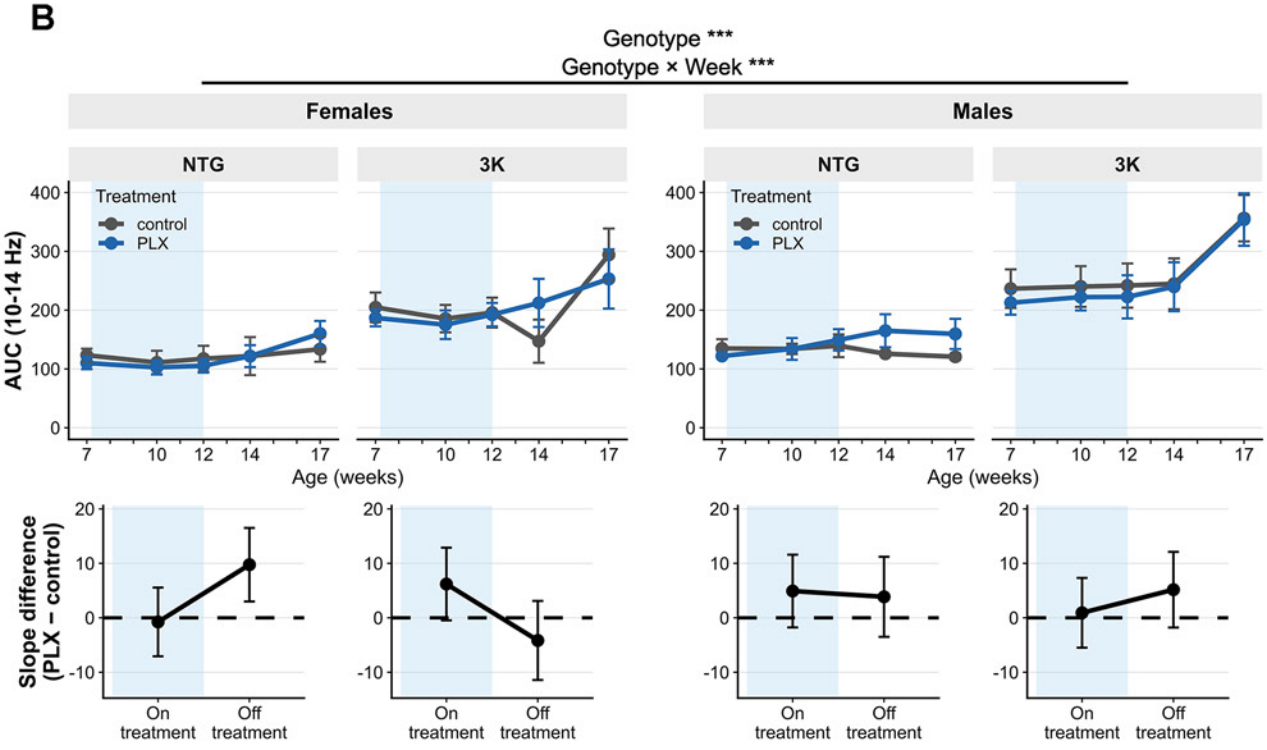

D
VEGFB_NRP1
VCAN_ITGB1
TIMP2_ITGB1
TIMP2_ITGA3
TGFB2_TGFBR1
TF_TFRC
SNCA_LAG3
SERPINE2_LRP1
SEMA4D_PLXNB2
PTN_PLXNB2
PSAP_LRP1
LTBP3_ITGB5
LTBP1_ITGB5
LPL_VLDLR
LPL_LRP1
LGALS1_ITGB1
LAMB1_ITGB1
L1CAM_CD9
ITGB2_THY1
GNAS_CRHR1
GNAI2_IGF1R
GNAI2_C5AR1
GNAI2_ADCY1
FNDC5_ITGB5
FBN1_ITGB1
CX3CL1_CX3CR1
CD9_L1CAM
CCL7_ACKR4
CCL2_ACKR4
CCL2_ACKR1
C1QB_LRP1
ARF1_INSR
ARF1_CHRM3
ADAM9_ITGB5
ADAM15_ITGB1
DAMs→SNc
DAMs→VTA
immune_cells→SNc
immune_cells→VTA
microglia→SNc
microglia→VTA
SNc→DAMs
SNc→immune_cells
SNc→microglia
VTA→DAMs
VTA→immune_cells
VTA→microglia
log2FC specificity
(CTRL/3K)
2
1
0
-1
-2

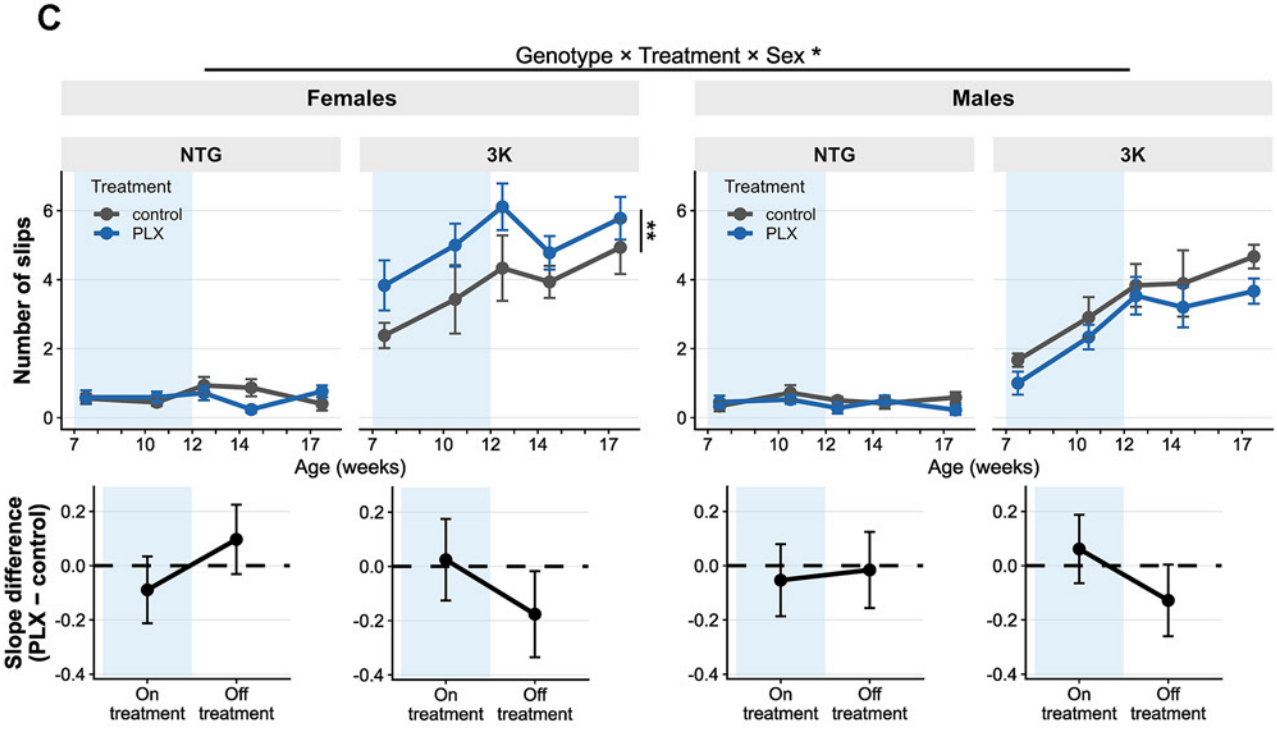
Suppl.Fig 6


A
3K het
Control
7 weeks
7 weeks
Gal3 Iba1 TH
B
3K het normal diet
3K het PLX3397
Control normal diet
Control PLX3397
22 weeks
22 weeks
22 weeks
22 weeks
Gal3 Iba1 DAPI

Suppl.Fig 7


A
Females
Males
Time to fall (sec)
Age (weeks)
***
*
plx food ctrl
plx food 3K
normal food ctrl
normal food 3K


B
Genotype ***
Genotype × Week ***
Females
Males
NTG
3K
Treatment
control
PLX
AUC (10-14 Hz)
Age (weeks)
Slope difference (PLX – control)
On treatment
Off treatment


C
Genotype × Treatment × Sex *
Females
Males
NTG
3K
Treatment
control
PLX
Number of slips
**
Age (weeks)
Slope difference (PLX – control)
On treatment
Off treatment