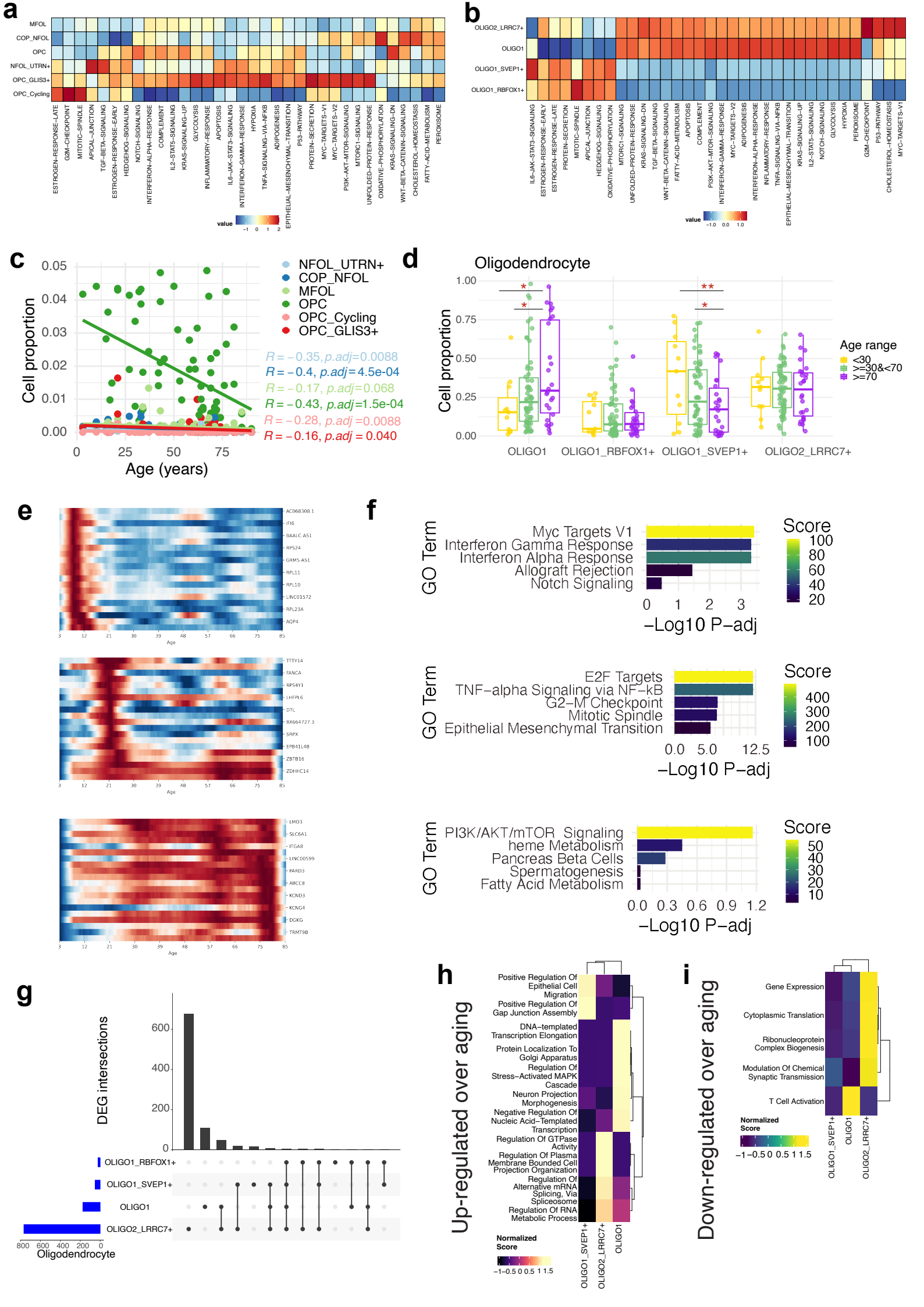
a
MFOL
COP_NFOL
OPC
NFOL_UTRN+
OPC_GLIS3+
OPC_Cycling
ESTROGEN−RESPONSE−LATE
G2M−CHECKPOINT
MITOTIC−SPINDLE
APICAL−JUNCTION
TGF−BETA−SIGNALING
ESTROGEN−RESPONSE−EARLY
HEDGEHOG−SIGNALING
NOTCH−SIGNALING
INTERFERON−ALPHA−RESPONSE
COMPLEMENT
IL2−STAT5−SIGNALING
KRAS−SIGNALING−UP
GLYCOLYSIS
INFLAMMATORY−RESPONSE
APOPTOSIS
IL6−JAK−STAT3−SIGNALING
INTERFERON−GAMMA−RESPONSE
HYPOXIA
TNFA−SIGNALING−VIA−NFKB
ADIPOGENESIS
EPITHELIAL−MESENCHYMAL−TRANSITION
P53−PATHWAY
PROTEIN−SECRETION
MYC−TARGETS−V1
MYC−TARGETS−V2
PI3K−AKT−MTOR−SIGNALING
MTORC1−SIGNALING
UNFOLDED−PROTEIN−RESPONSE
OXIDATIVE−PHOSPHORYLATION
KRAS−SIGNALING−DN
WNT−BETA−CATENIN−SIGNALING
CHOLESTEROL−HOMEOSTASIS
FATTY−ACID−METABOLISM
PEROXISOME
value
−1 0 1 2
b
OLIGO2_LRRC7+
OLIGO1
OLIGO1_SVEP1+
OLIGO1_RBFOX1+
IL6−JAK−STAT3−SIGNALING
ESTROGEN−RESPONSE−EARLY
ESTROGEN−RESPONSE−LATE
PROTEIN−SECRETION
MITOTIC−SPINDLE
APICAL−JUNCTION
HEDGEHOG−SIGNALING
OXIDATIVE−PHOSPHORYLATION
UNFOLDED−PROTEIN−RESPONSE
MTORC1−SIGNALING
KRAS−SIGNALING−DN
TGF−BETA−SIGNALING
WNT−BETA−CATENIN−SIGNALING
FATTY−ACID−METABOLISM
APOPTOSIS
COMPLEMENT
PI3K−AKT−MTOR−SIGNALING
INTERFERON−GAMMA−RESPONSE
MYC−TARGETS−V2
ADIPOGENESIS
INTERFERON−ALPHA−RESPONSE
INFLAMMATORY−RESPONSE
TNFA−SIGNALING−VIA−NFKB
EPITHELIAL−MESENCHYMAL−TRANSITION
KRAS−SIGNALING−UP
IL2−STAT5−SIGNALING
NOTCH−SIGNALING
GLYCOLYSIS
HYPOXIA
PEROXISOME
G2M−CHECKPOINT
P53−PATHWAY
CHOLESTEROL−HOMEOSTASIS
MYC−TARGETS−V1
value
−1.0 0.0 1.0
c
Cell proportion
0.05
0.04
0.03
0.02
0.01
0.00
0
25
50
75
Age (years)
NFOL_UTRN+
COP_NFOL
MFOL
OPC
OPC_Cycling
OPC_GLIS3+
R = −0.35, p.adj=0.0088
R = −0.4, p.adj = 4.5e-04
R = −0.17, p.adj=0.068
R = −0.43, p.adj =1.5e-04
R = −0.28, p.adj =0.0088
R = −0.16, p.adj = 0.040
d
Oligodendrocyte
Cell proportion
1.00
0.75
0.50
0.25
0.00
OLIGO1
OLIGO1_RBFOX1+
OLIGO1_SVEP1+
OLIGO2_LRRC7+
Age range
<30
>=30&<70
>=70
e
AC068308.1
IFI6
BAALC−AS1
RPS24
GRM5−AS1
RPL11
RPL10
LINC01572
RPL23A
AQP4
Age
TTTY14
FANCA
RPS4Y1
LHFPL6
DTL
BX664727.3
SRPX
EPB41L4B
ZBTB16
ZDHHC14
Age
LMO3
SLC6A1
ITGA8
LINC00599
PARD3
ABCC8
KCND3
KCNG4
DGKG
TRMT9B
Age
f
GO Term
Myc Targets V1
Interferon Gamma Response
Interferon Alpha Response
Allograft Rejection
Notch Signaling
0 1 2 3
−Log10 P−adj
Score
100
80
60
40
20
GO Term
E2F Targets
TNF−alpha Signaling via NF−kB
G2−M Checkpoint
Mitotic Spindle
Epithelial Mesenchymal Transition
0.0 5.0 12.5
−Log10 P−adj
Score
400
300
200
100
GO Term
PI3K/AKT/mTOR Signaling
heme Metabolism
Pancreas Beta Cells
Spermatogenesis
Fatty Acid Metabolism
0.0 0.3 0.6 0.9 1.2
−Log10 P−adj
Score
50
40
30
20
10
g
DEG intersections
600
400
200
0
OLIGO1_RBFOX1+
OLIGO1_SVEP1+
OLIGO1
OLIGO2_LRRC7+
800 600 400 200 0
Oligodendrocyte
h
Up−regulated over aging
Positive Regulation Of Epithelial Cell Migration
Positive Regulation Of Gap Junction Assembly
DNA−templated Transcription Elongation
Protein Localization To Golgi Apparatus
Regulation Of Stress−Activated MAPK Cascade
Neuron Projection Morphogenesis
Negative Regulation Of Nucleic Acid−Templated Transcription
Regulation Of GTPase Activity
Regulation Of Plasma Membrane Bounded Cell Projection Organization
Regulation Of Alternative mRNA Splicing, Via Spliceosome
Regulation Of RNA Metabolic Process
Normalized Score
−1 −0.5 0 0.5 1 1.5
OLIGO1_SVEP1+
OLIGO2_LRRC7+
OLIGO1
i
Down−regulated over aging
Gene Expression
Cytoplasmic Translation
Ribonucleoprotein Complex Biogenesis
Modulation Of Chemical Synaptic Transmission
T Cell Activation
Normalized Score
−1 −0.5 0 0.5 1 1.5
OLIGO1_SVEP1+
OLIGO1
OLIGO2_LRRC7+

Figure 4. Functional state and age-related changes of oligodendrocytes and their precursors.

a, Heatmap showing the biological processes and pathways enriched in each oligodendrocyte precursor population. **b,** Heatmap showing the biological processes and pathways enriched in each oligodendrocyte subtype. **c**, Scatter plot showing cell proportions (Y-axis) of the oligodendrocyte precursor populations associated with age (X-axis). The pearson correlation coefficient (*R*) and *P.adj* after multiple testing correction from multivariable linear regression (*p*) were indicated. **d**, Box plot showing cell composition across three age ranges within oligodendrocyte populations. *: $P < 0.05$, **: $P<0.01$ **e**, Heatmap showing changes in gene expression (Y-axis) across age (X-axis). **f**, Bar plot showing biological processes enriched in age-related gene modules identified in Fig. 4e. **g**, UpSet plot showing the number of age-related differentially expressed genes (DEG) identified in each oligodendrocyte subtype. **h,** Heatmap showing the biological processes enriched among DEGs up-regulated with age. **i,** Heatmap showing the biological processes enriched among DEGs down-regulated with age.