Fig. S1

A

Rembrandt

NTEM^lowPM^low   PM+++   EM++   EM+++

-2   0   2

B

GSE9566

Developing Astrocyte   Mature Astrocyte   Mature Neuron   Mature OL   Developing OL

Astros P7 (5a)
Astros P7 (6a)
Astros P8 (7a)
Astros P1 (34a)
Astros P17 (22a)
Astros P17 (24a)
Astros P17g (32a)
Astros P17g (25g)
Astros P17g (36g)
Astros P30 (33a)
Neurons P16 (10d)
Neurons P16 (11d)
Neurons P16n (13b)
Neurons P26 (18b)
Neurons P7 (5b)
Neurons P7 (6b)
Neurons P7 (8b)
Neurons P7n (38B)
Myelin OLs (30q)
Myelin OLs (MOG_a2)
Myelin OLs (MOG_b)
Myelin OLs (MOG_c)
OLs (30p)
OLs (GC_a3)
OLs (GC_b)
OLs (GC_c)

-2   0   2

C

Absolute_Purity

NS.

***

***

EM (N = 206)
PM (N = 295)
EM^lowPM^low (N = 55)

1.25
1.00
0.75
0.50
0.25

D

EM   PM   EM^lowPM^low

NeuN   NeuN   NeuN

|	EM	PM	EM^lowPM^low
N	5	4	10
Weak Positive	0	4	2
Strong Positive	0	0	7

Supplementary Fig. S1 Identification of glioma samples highly contaminated with NT brain tissues.

(A) Identification of 35 genes enriched in NT brain tissues.
Heatmap for the expression profile of the NT identifier across the epileptic brain tissues (the NT samples), glioma samples with an $EM^{low}PM^{low}$, PM or EM phenotype at q = 0.01 is shown.
(B) Enriched expression of NT identifier in mature neuron.
Hierarchical clustering between the NT identifier and neural cells was performed in murine neural cell transcriptome dataset GSE9566. Heatmap of the expression pattern of NT identifier across neural cell populations is shown.
(C) Low purity in samples with high expression of the NT identifier and low expression of the EM and PM modules. ABSOLUTE analysis was performed with the WES data for the TCGA samples. ***: p < 0.001, Mann-Whitney test.
(D) Glioma samples with the $EM^{low}PM^{low}$ signature contain large proportion of NT brain tissues.
Images of NeuN (RBFOX3) staining in representative EM, PM or $EM^{low}PM^{low}$ samples are shown.
Samples were derived from the CGGA dataset as depicted in Figure 1A.

Fig. S2

A

CGGA (N = 325), K = 3

B
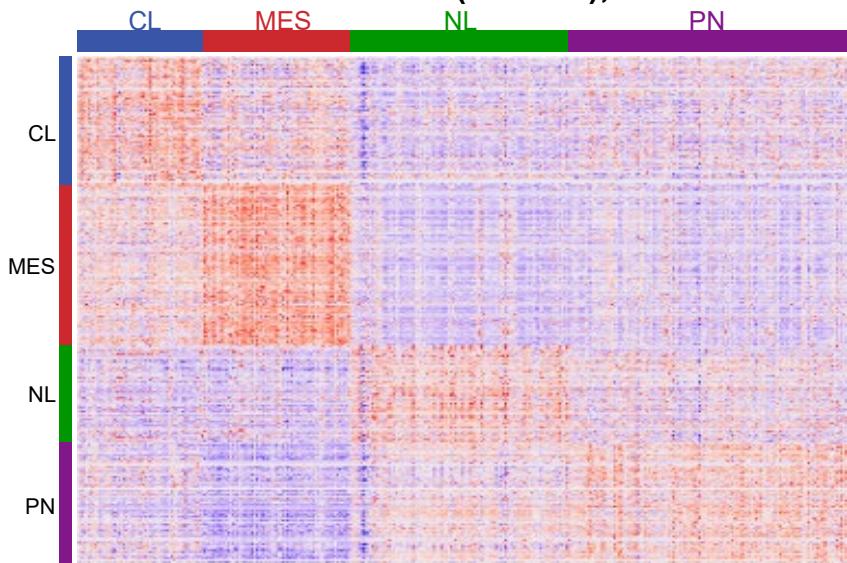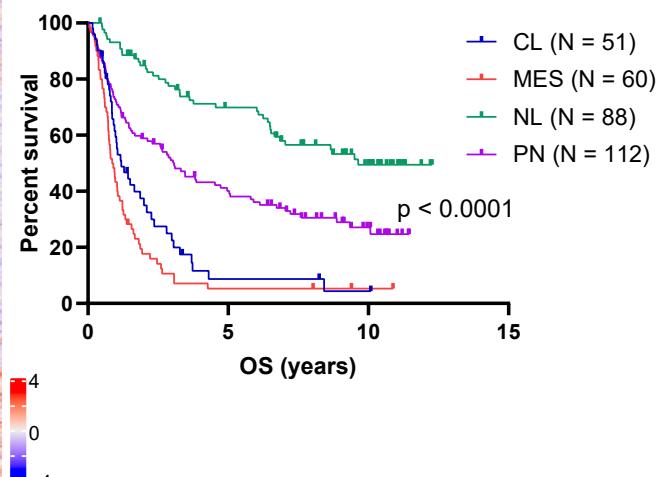
TCGA (N = 701), K = 3
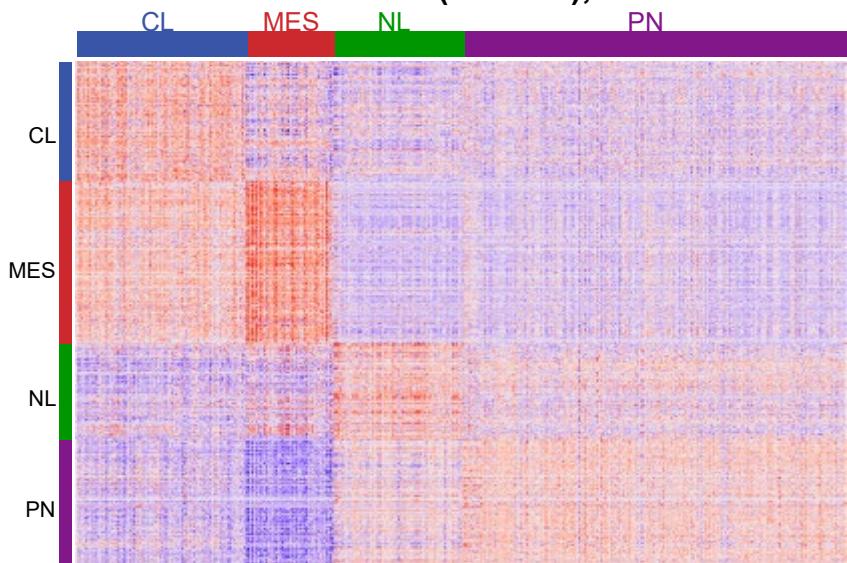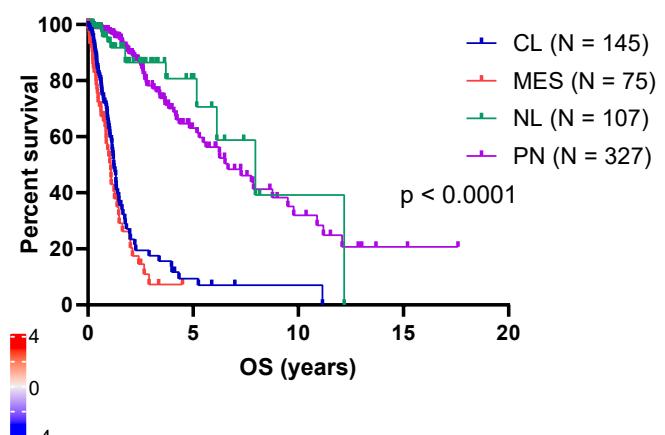
C

TCGA clusters	EM/PM clusters		
CGGA			
	EM	PM	$EM^{low}PM^{low}$
CL	48	4	1
MES	52	2	8
NL	4	45	43
PN	0	115	3
TCGA			
	EM	PM	$EM^{low}PM^{low}$
CL	147	7	0
MES	71	7	2
NL	10	37	71
PN	7	338	4

Supplementary Fig. S2 Cross-lalelling analysis between EM/PM classification and TCGA subtyping in the CGGA and TCGA datasets.

(A and B) Left: heatmap of TCGA identifier in the transcriptome of 325 CGGA or 701 TCGA adult gliomas. Right: Kaplan–Meier plots of OS for the TCGA subtypes are shown.
(C) Cross-labeling analysis between the EM/PM subtypes and the TCGA subtypes in the CGGA and TCGA datasets.

Fig. S3

A Metagene Projection

EM (N = 65)   PM (N = 32)

Primary   61   26

93.8%   81.3%

Recurrent   61   26

B Centroid-based SSP

EM (N = 65)   PM (N = 44)

Primary   57   36

87.7%   81.8%

Recurrent   57   36

EM (N = 47)
PM (N = 5)
p = 0.011

EM (N = 47)
PM (N = 10)
p = 0.002

C
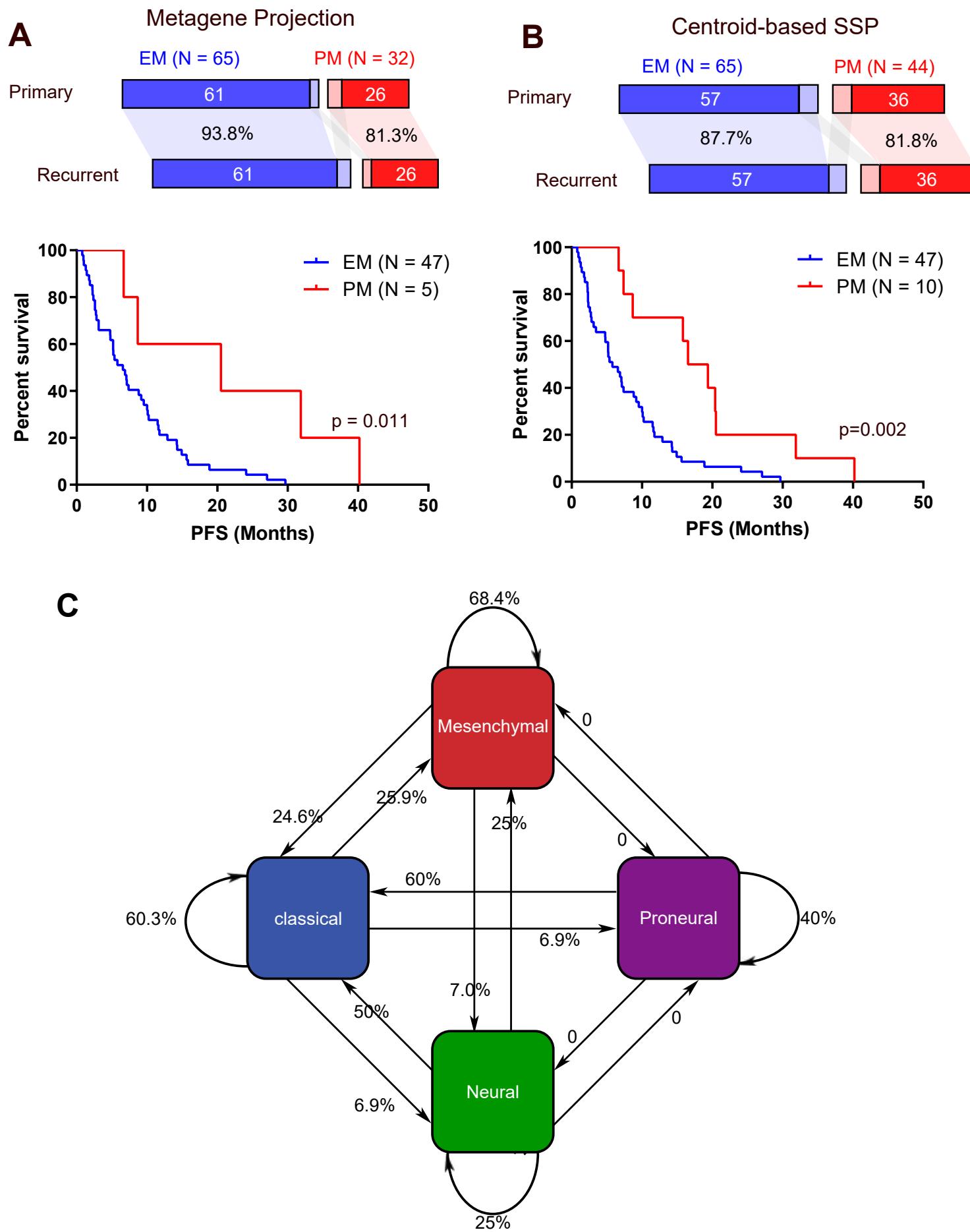
Supplementary Fig. S3 Stability of the EM/PM subtypes but shifting TCGA subtypes in the same cohorts of the paired longitudinal samples.

(A and B) The EM/PM subtypes were assigned using metagene projection (A) or centroid-based SSP (B) approach in the transcriptomes of the paired longitudinal higher degree gliomas. Results of cross-labelling between the primary and recurrent samples and Kaplan-Meier plots for subtype-specific PFS are shown. Samples were derived from TCGA [56] or other institutions [13,20-23].
(C) Metagene projection analysis was used to assign the same cohorts analyzed in (A) and (B) into the classical, neural, mesenchymal or proneural subtypes. The frequencies with a maintained or changed subtyping result between the paired primary and recurrent gliomas are shown.

Fig. S4
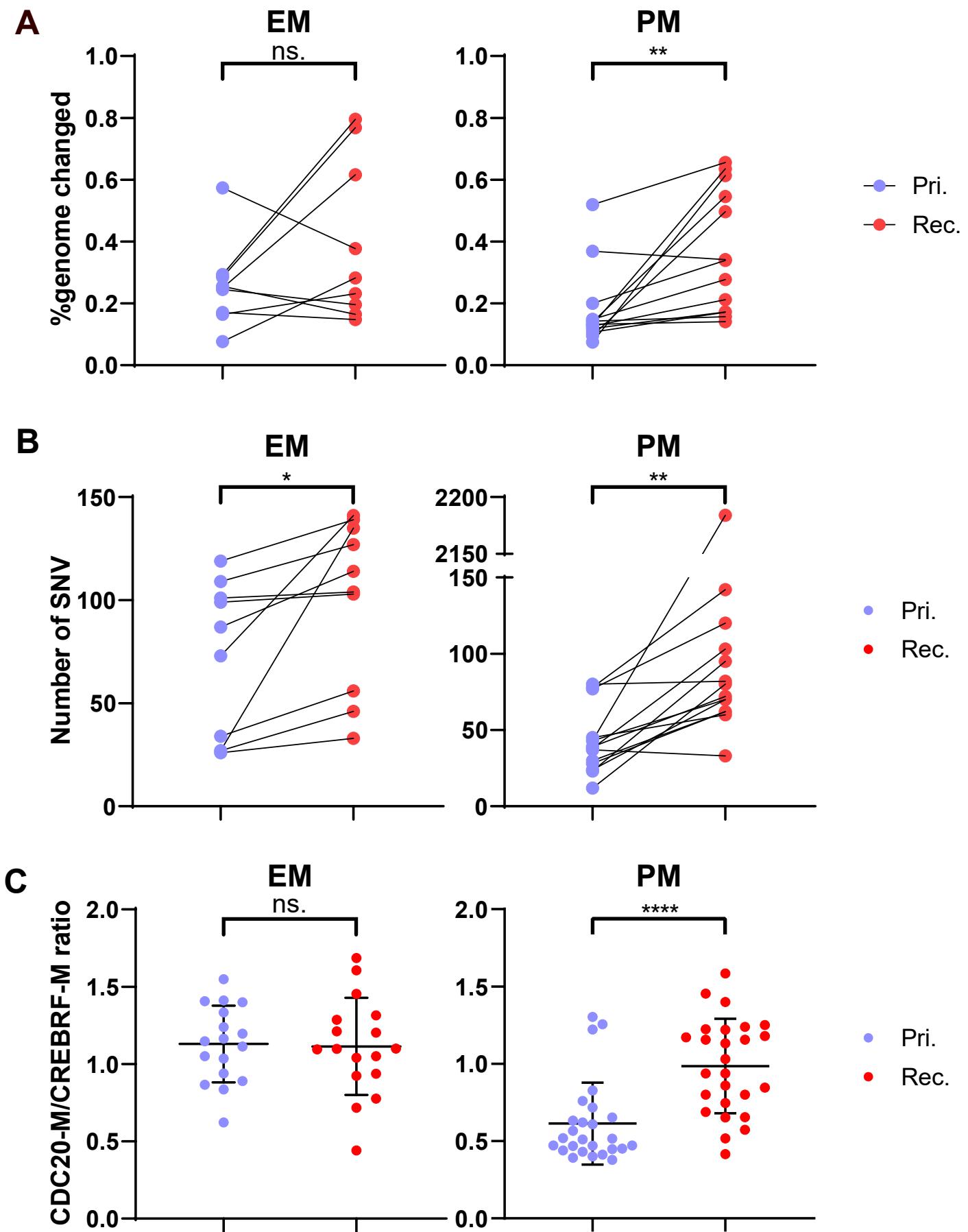
Supplementary Fig. S4 Extensive genomic instability and elevated CDC20-M expression in the recurrent gliomas.

(A) Elevated CNVs in the recurrent PM gliomas (EM: 9 pairs, p = 0.143; PM: 13 pairs, p = 0.005, paired t-test).

(B) Elevated SNVs in the recurrent gliomas (EM: 9 pairs, p = 0.020; PM: 13 pairs, p = 0.004, paired t-test).

(C) Elevated CDC20-M expression in recurrent PM gliomas (EM: 17 pairs, p = 0.856; PM: 25 pairs, p < 0.0001, paired t-test).

Data are derived from combined analysis of the paired primary (Pri) and recurrent (Rec) samples from CGGA and TCGA.

Fig. S5
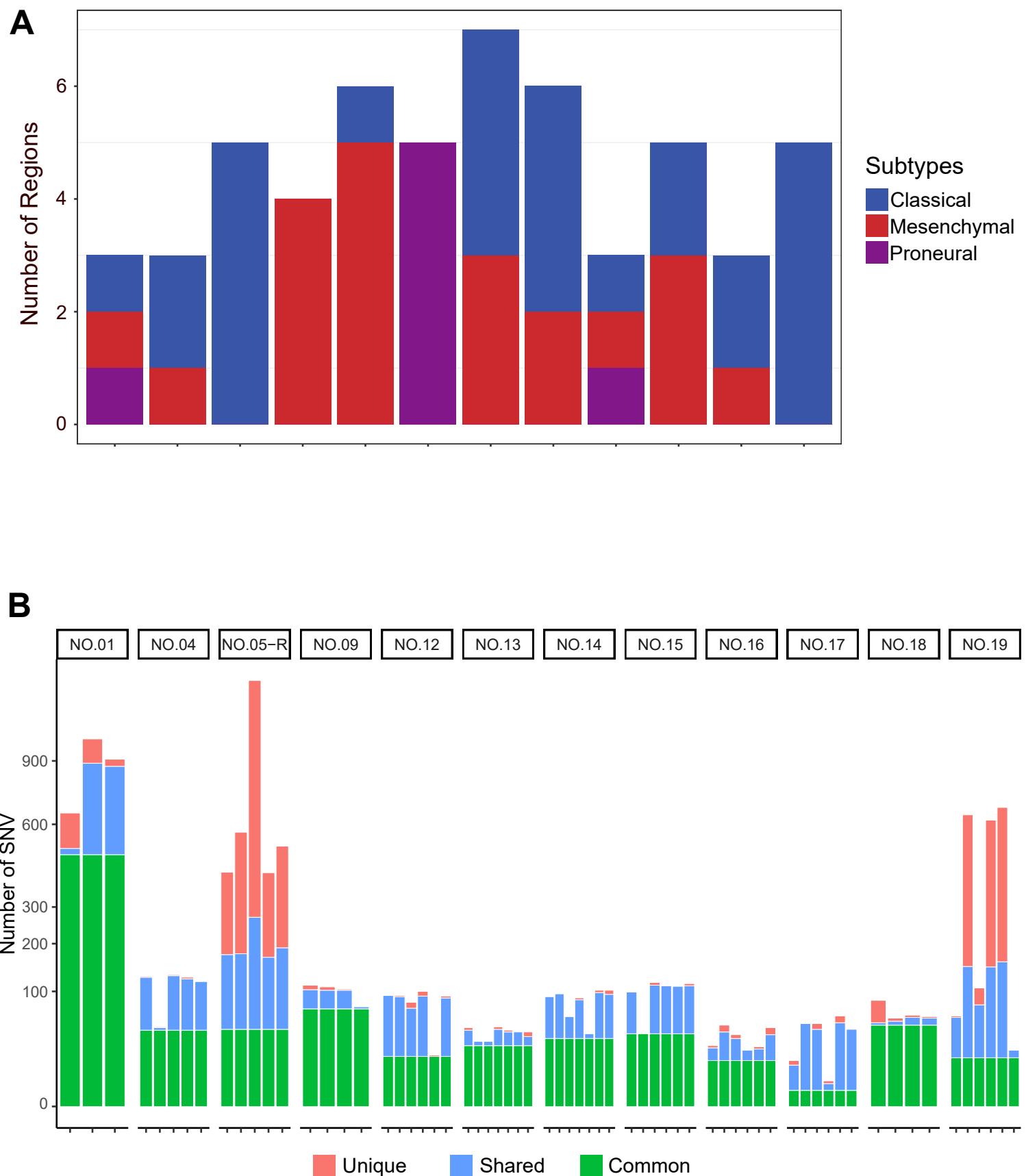
Supplementary Fig. S5 Co-existence of more than one TCGA subtypes and region-specific SNVs in the multiregional samples from CGGA.

(A) RNA-seq data from the multi-regional samples analyzed in Fig 3A were subtyped according to the TCGA classification scheme using both metagene projection and centroid-based SSP, more than one subtypes were found in 8 of the 12 gliomas analyzed.

(B) Summary of SNVs unique to each region, shared in more than one but not all regions, and common in all regions across the multiregional samples.

Fig. S6

GSE70630

A

B SOX2

Proportional expression z-scores

C

OL
Microglia
PM

EM PM MG OL

D PM TME

inferCNV

E

References(Cells)

Microglia
OL

Observation(Cells)

PM

chr 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

F

Average expression

Percent Expressed

EM PM
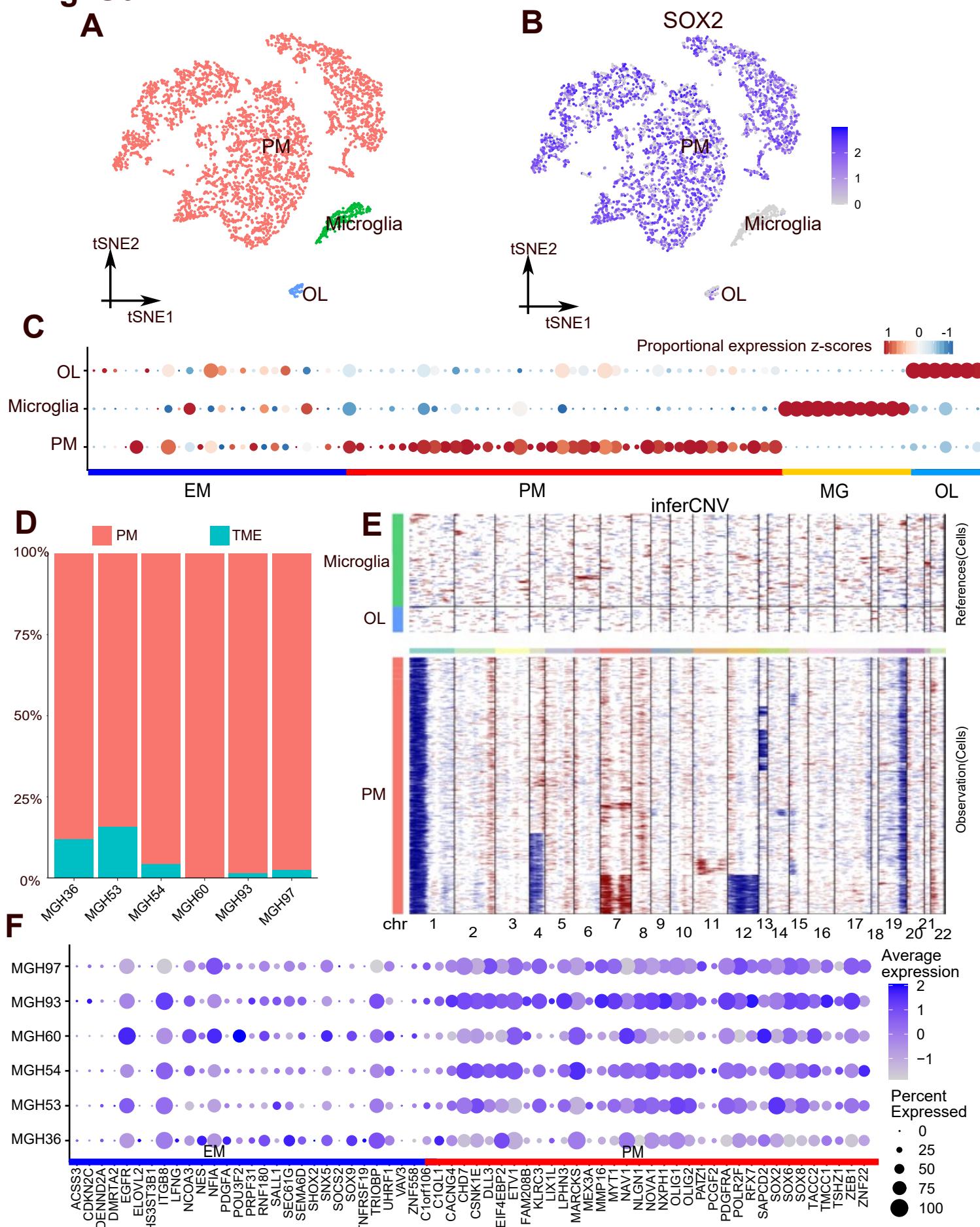
Supplementary Fig. S6 Expression of the EM and PM signatures in single cells from IDH-mutant gliomas with 1p19q co-deletion in dataset GSE70630.

(A) t-SNE plot of cell populations identified.

(B) Overlay of SOX2 expression on t-SNE plot.

(C) Differential expression of EM/PM signatures and canonical markers of non-malignant cells across the cell populations in the dataset.

(D) Frequencies of cell subtypes in individual samples. OL and microglia were assigned into the TME fraction.

(E) CNV profiles in the malignant cell populations identified, OL and microglia served as the control.

(F) Concordant expression of the PM members but sporadic expression of the EM members in the malignant cells in individual samples.

Fig. S7

A GSE89567

B SOX2

C Proportional expression z-scores

EM | PM | MG | OL

inferCNV

D PM | TME

E References(Cells) / Observation(Cells)

chr 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22

F Average expression / Percent Expressed

EM | PM
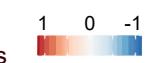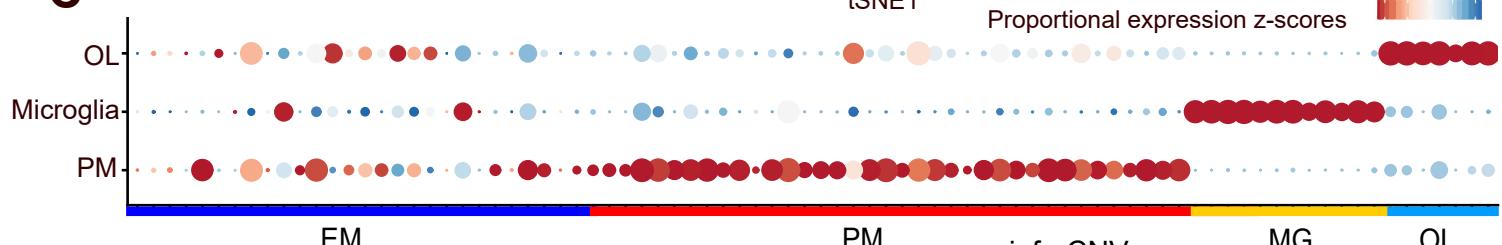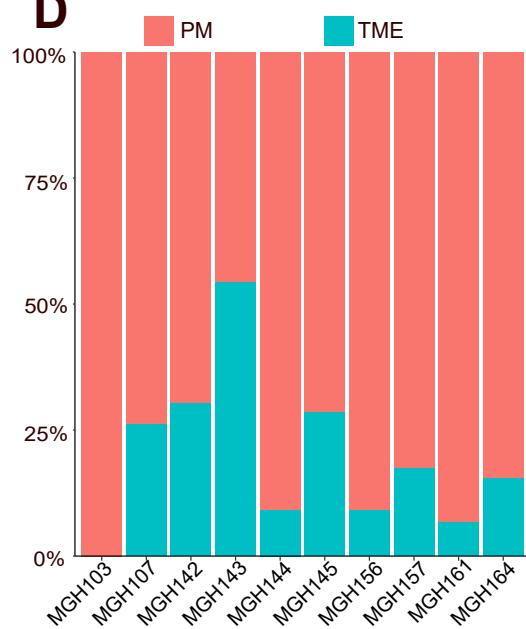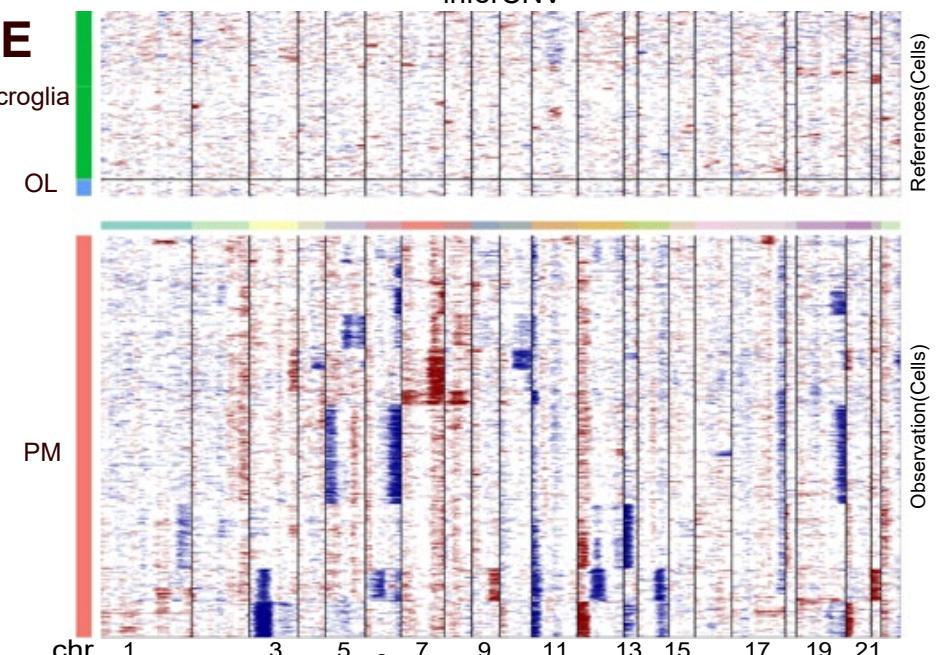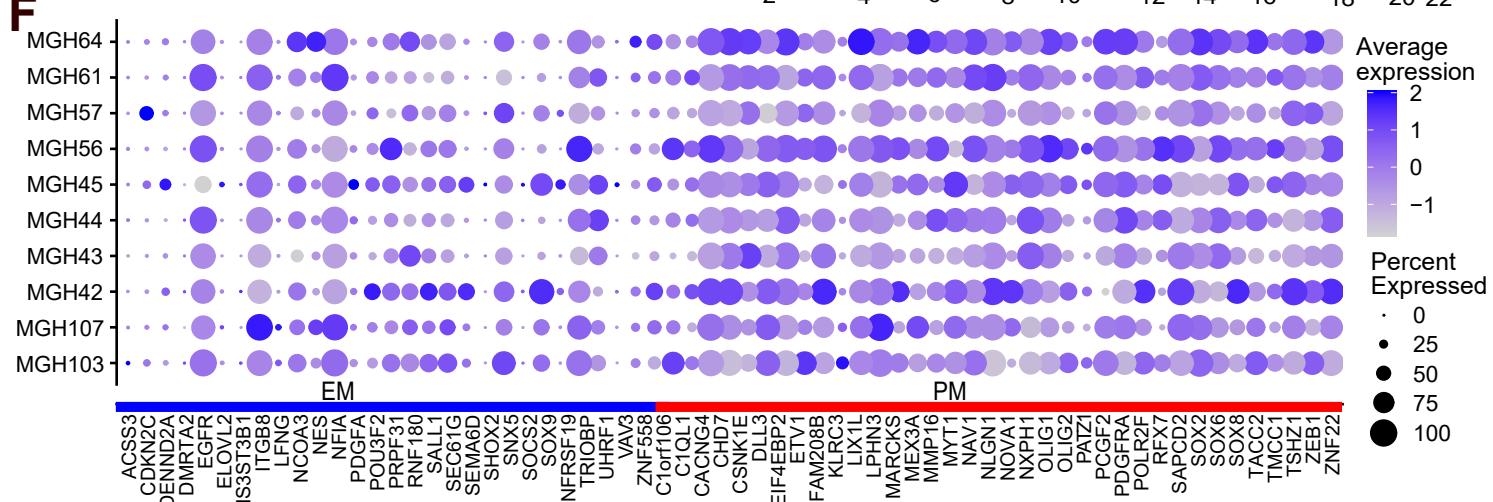
Supplementary Fig. S7 Expression of the EM and PM signatures in single cells from IDH-mutant gliomas without 1p19q co-deletion in dataset GSE89567.

(A) t-SNE plot of cell populations identified.

(B) Overlay of SOX2 expression on t-SNE plot.

(C) Differential expression of EM/PM signatures and canonical markers of non-malignant cells across the cell populations in the dataset.

(D) Frequencies of cell subtypes in individual samples. OL and microglia were assigned into the TME fraction.

(E) CNV profiles in the cell populations identified, OL and microglia served as the control.

(F) Concordant expression of the PM members but sporadic expression of the EM members in the malignant cells in individual samples.

Fig. S8

GSE131928

A

Mf/MG
EM++
T cell
OL
EM+PM++
tSNE2
tSNE1

B

SOX2
Mf/MG
EM++
T cell
OL
EM+PM++
tSNE2
tSNE1

Proportional expression z-scores

C

T cell
OL
Mf/MG
EM++
EM+PM++

EM   PM   MG   Mf   T cell   OL

D

EM++   EM+PM++   TME

E

inferCNV

MG/Mf
OL
T cell
References(Cells)

EM+PM++
EM++
Observation(Cells)

chr   1   2   3   4   5   6   7   8   9   10 11 12 13 14 15 16 17 18 19 20 21 22

F

MGH 100   EM++   EM+PM++
MGH 115   EM++   EM+PM++
MGH 125   EM++   EM+PM++

Average Expression
Percent Expressed
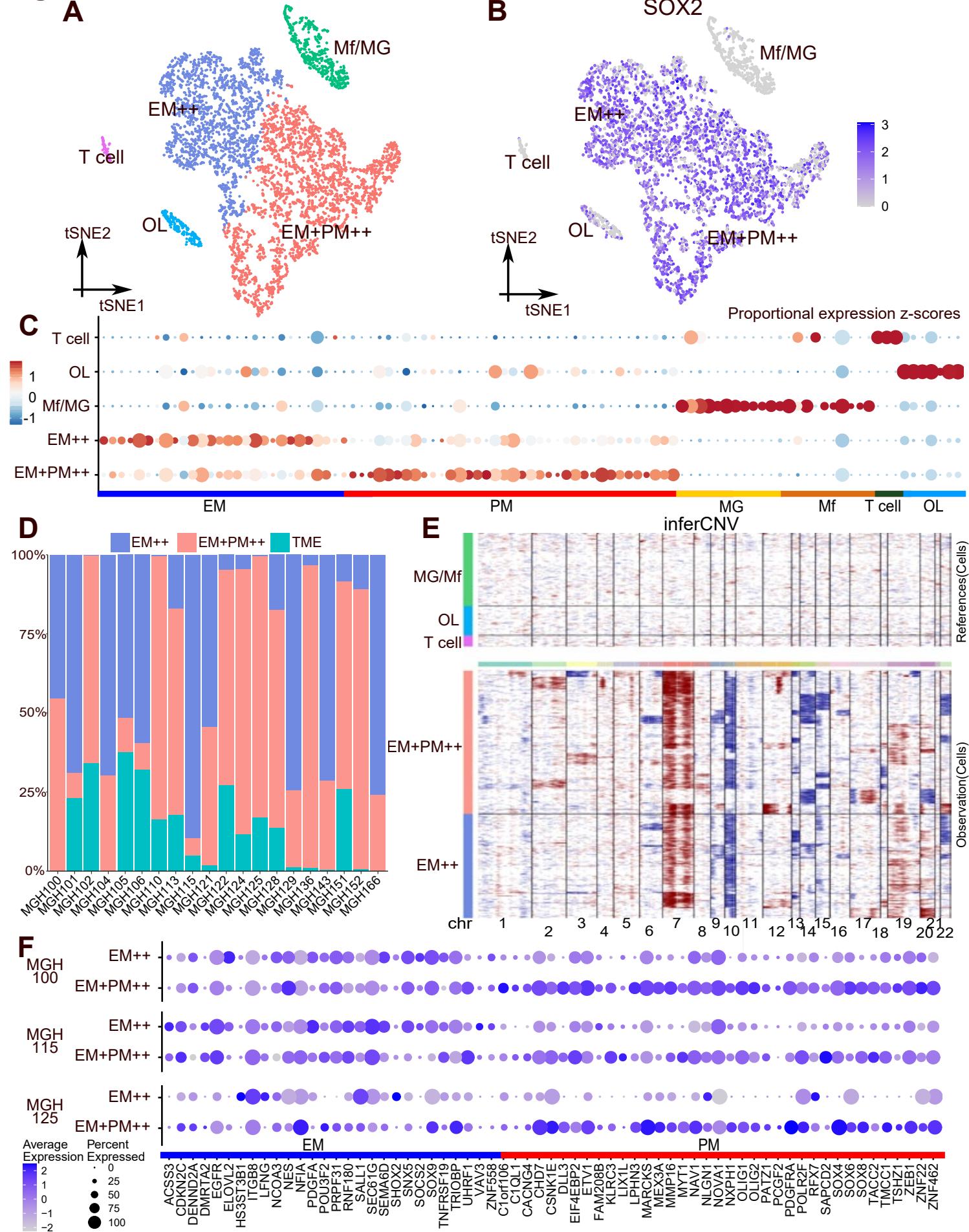
EM   PM

Supplementary Fig. S8 Expression of the EM and PM signatures in single cells from IDH-WT gliomas in dataset GSE131928.

(A) t-SNE plot of cell populations identified.

(B) Overlay of SOX2 expression on t-SNE plot.

(C) Differential expression of EM/PM signatures and canonical markers of non-malignant cells across the cell populations in the dataset.

(D) Frequencies of cell subtypes in individual samples. OL, Mf/MG, and T cell were assigned into the TME fraction.

(E) CNV profiles in the cell populations identified, OL, Mf/MG, and T cell served as control.

(F) Expression profile of the EM and PM signatures in the malignant cells in representative samples. The EM+PM++ cells were enriched in concordant expression of PM members on the background of co-expression of EM members.

Fig. S9

A   TCGA, EM (N = 235)

consensus matrix k=2

B   CGGA, EM (N = 104)

consensus matrix k=2

N	69	166
7 gain/10 loss	40/65 (61.5%)	135/164 (82.3%)
Focal Amp *PDGFRA*	16/65 (24.6%)	23/164 (14.0%)
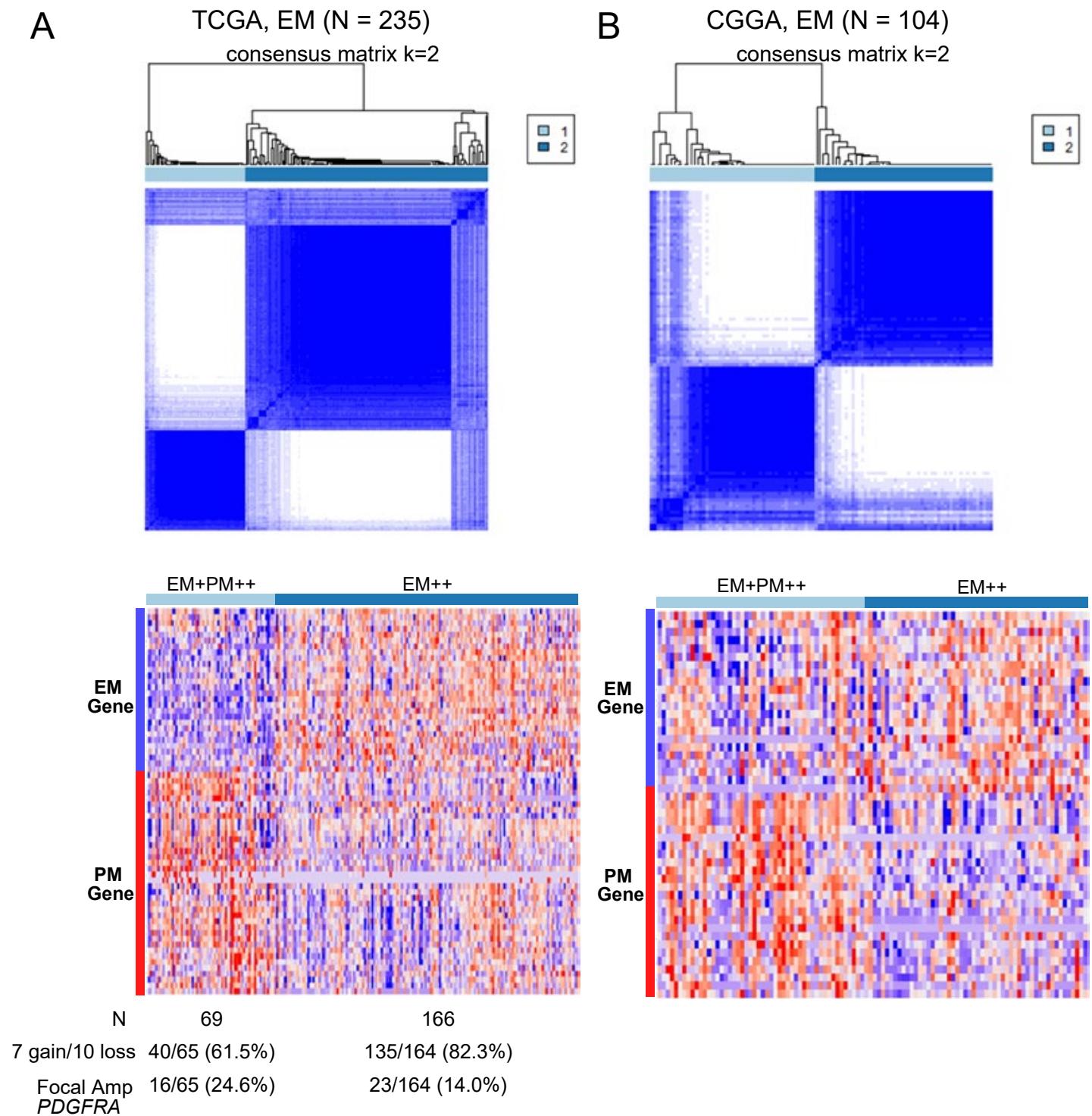
Supplementary Fig. S9 Expression of the EM and PM signatures in bulk transcriptome data of the EM gliomas.

Results of unsupervised consensus clustering between the EM gliomas of CGGA (**A**) or TCGA (**B**) cohort analyzed in Figure 1 and the EM/PM modules are shown. Upper: consensus matrices for K = 2; lower: heatmaps of the EM and PM expression across the EM gliomas and the frequencies of the concomitant gain of chromosome 7 and loss of chromosome 10, and focal amplification of *PDGFRA* locus.

Fig. S10

A

GSE117891
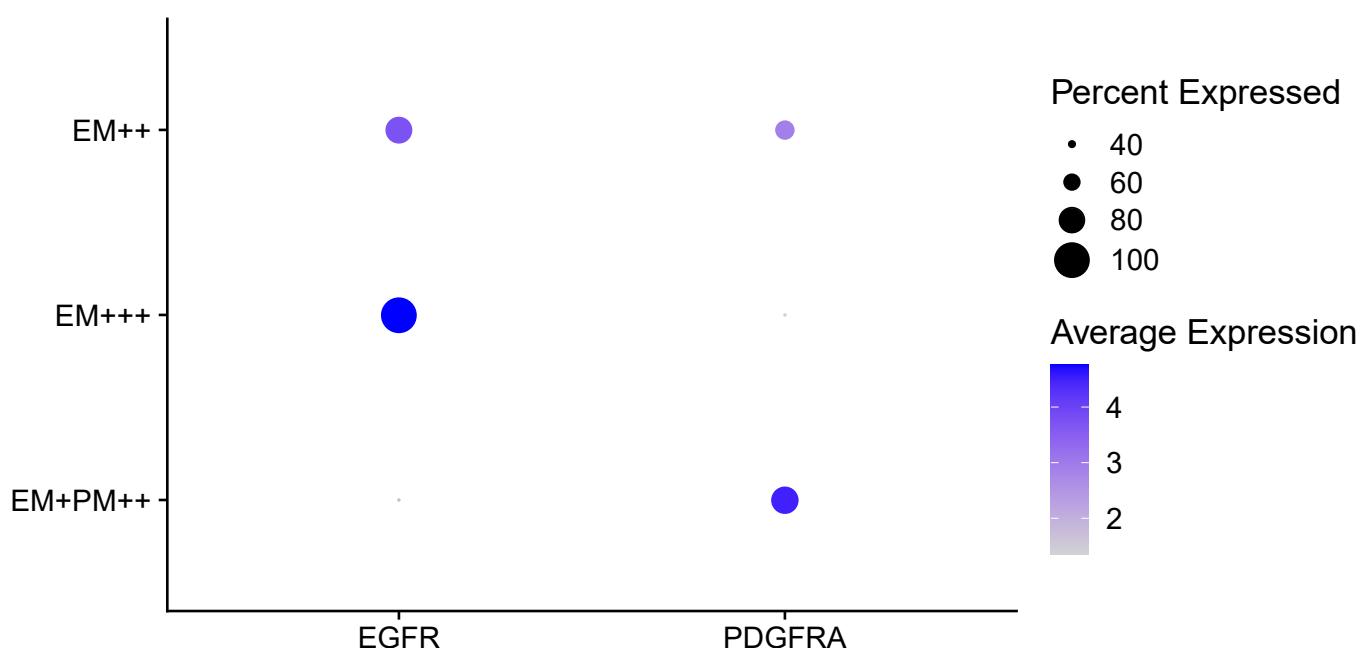
B

GSE131928
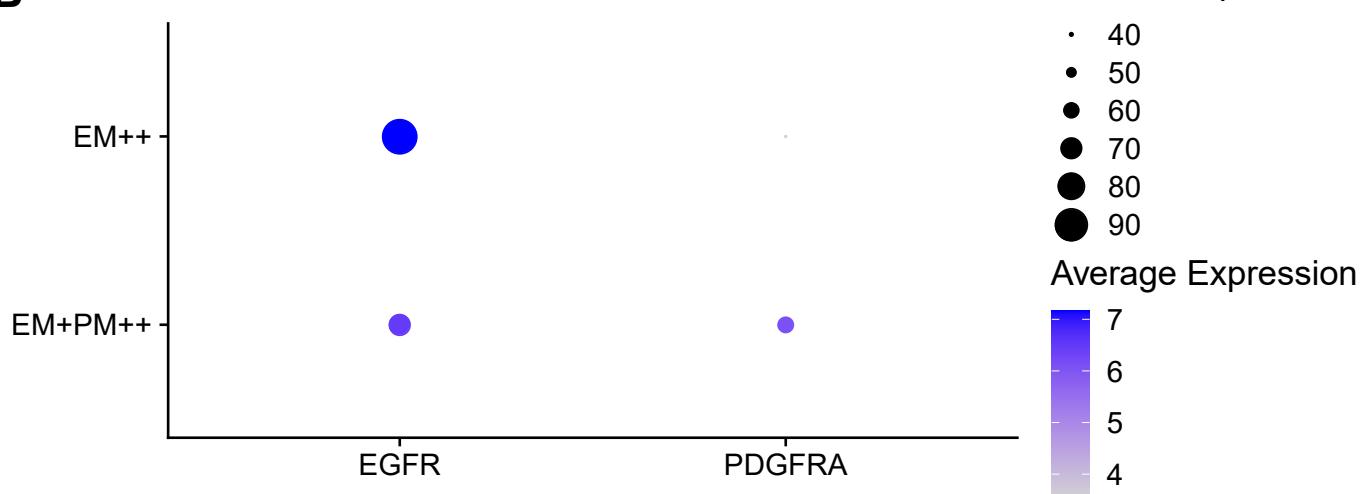
Supplementary Fig. S10 Reciprocal expression pattern between EGFR and PDGFRA in the malignant cell populations of IDH-WT gliomas.

(A) Normalized expression levels of EGFR and PDGFRA in the indicated cell populations from samples in our own dataset GSE117891.

(B) Normalized expression levels of EGFR and PDGFRA in the indicated cell populations from samples in the external dataset GSE131928.

Fig. S11

A

GSE117891

B

Merged 4 datasets
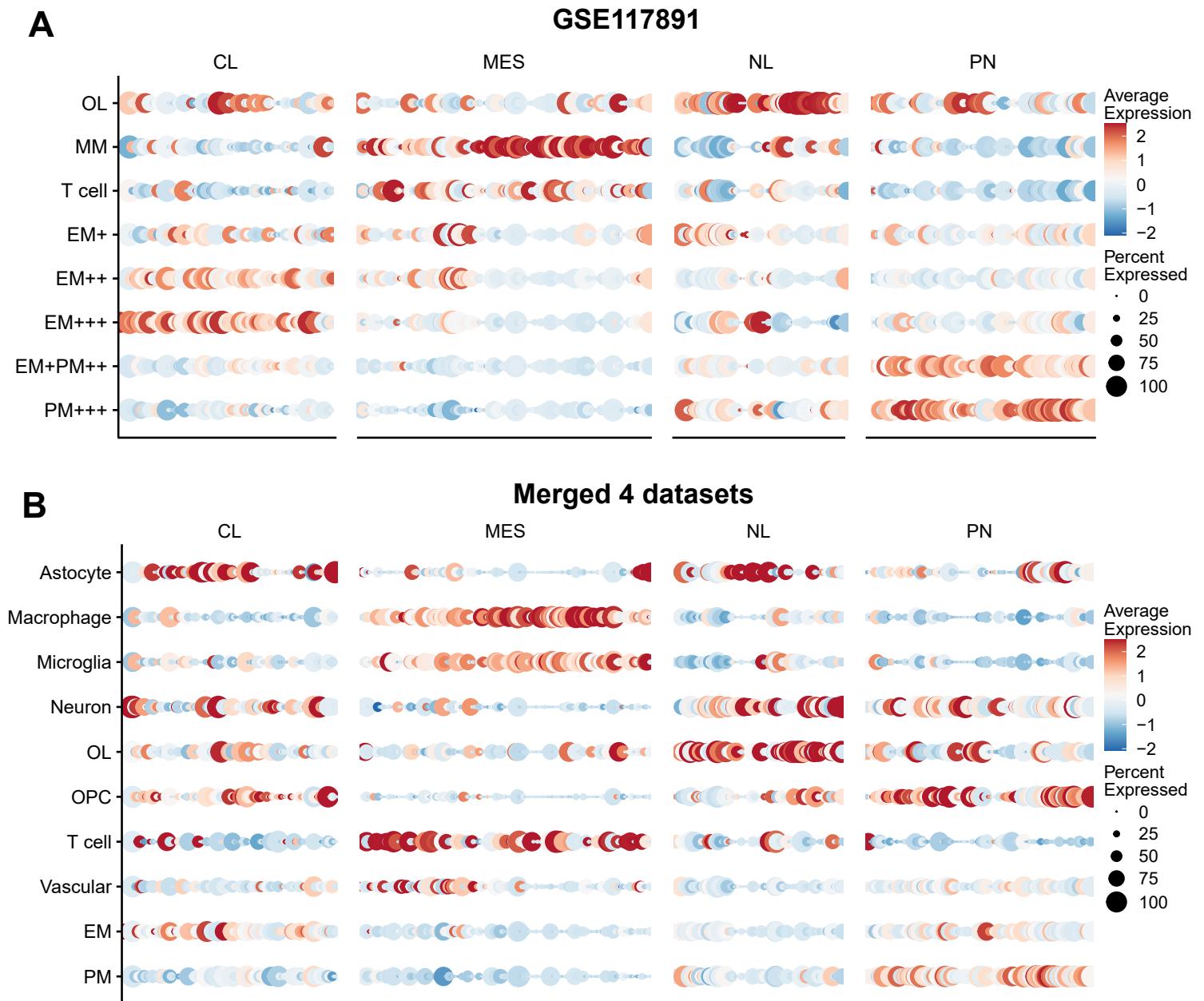
Supplementary Fig. S11 Expression profiles of the TCGA subtype classifiers across the cell populations inferred from single cell RNAseq data.

(A) Depiction of the expression profiles of the 148, 203, 119, and 154 classifier genes for the CL, MES, NL, and PN subtype, respectively, in GSE117891.

(B) Depiction of the expression profiles of the 152, 205, 123, and 160 classifier genes for the CL, MES, NL, and PN subtype, respectively, in an external dataset merged from GSE70630, GSE89567, GSE84465 and GSE131928.

Fig. S12
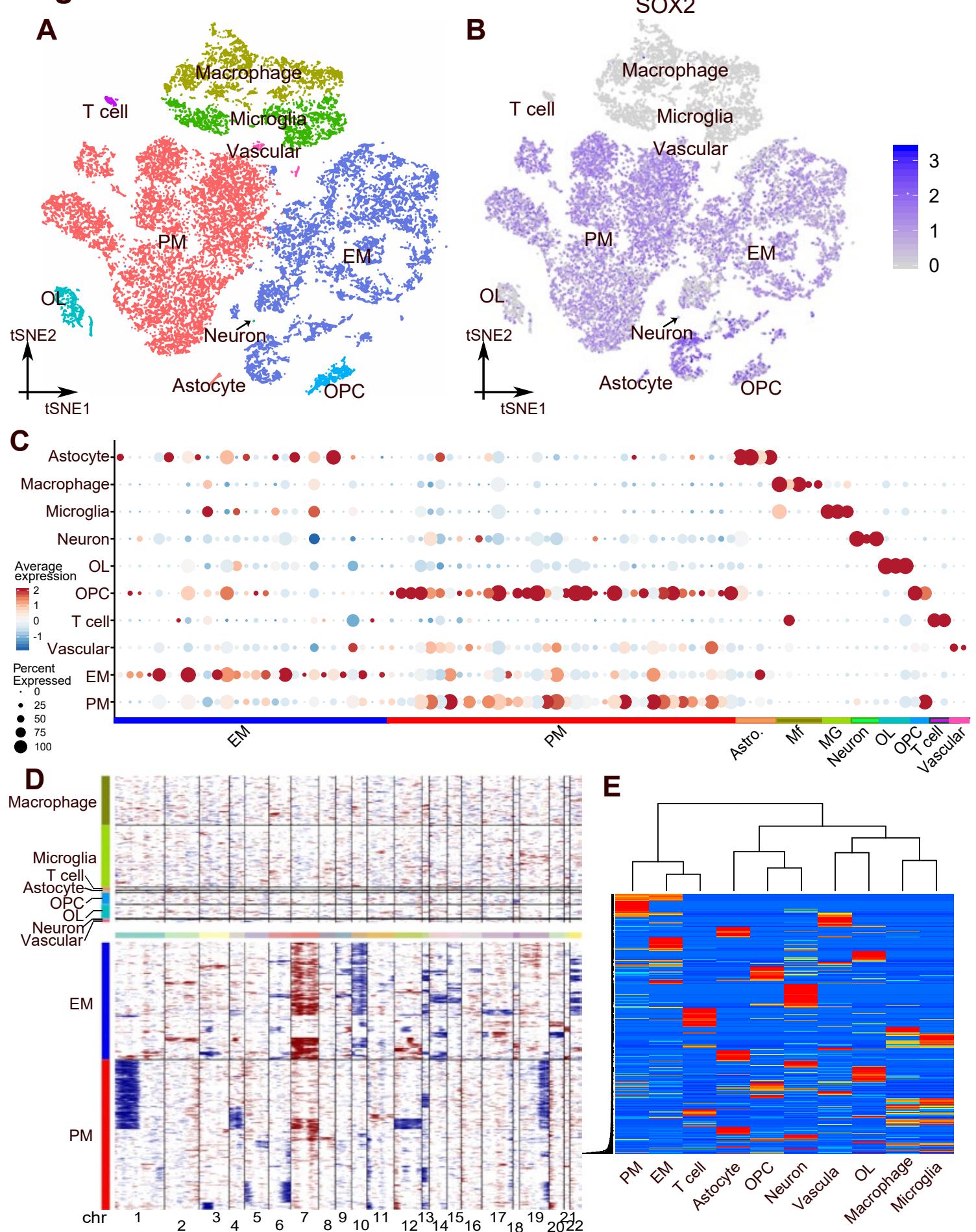
Supplementary Fig. S12 Cell populations identified in IDH-mutant gliomas and IDH-WT gliomas.

(A) t-SNE plot of cell populations identified.

(B) Overlay of SOX2 expression on t-SNE plot.

(C) Differential expression of canonical markers of non-malignant cells and the EM/PM signatures across the cell populations in the merged dataset.

(D) CNV profiles in the cell populations identified, non-malignant cell populations served as the control.

(E) Heatmap of the expression of signature genes across the cell populations identified.

SC-RNAseq data from *IDH*-mutant gliomas from GSE70630 and GSE89567 and *IDH*-WT gliomas from GSE84465 and GSE131928 were merged for identification of the cell populations and their signature genes using the Seurat platform.

Supplementary Table S1 Members of NT identifiers categorized according to gene ontology (GO) processes.

GO Term	Gene symbol
nervous system development	EPHA5, FEZF2, BDNF, OPA1, SSTR1, KCNAB1, CAMSAP1, SRD5A1, ATOH7, KLHL1
response to external stimulus	EPHA5, IL12RB2, GUCA1A, FEZF2, BDNF, SSTR1, SRD5A1, ATOH7
central nervous system development	EPHA5, FEZF2, SSTR1, KCNAB1, SRD5A1, KLHL1
cell-cell signaling	EPHA5, BDNF, SSTR1, GRM7, CCNY, SOX7
behavior	FEZF2, KCNAB1, GRM7, SRD5A1, KLHL1
protein localization	EPHA5, BDNF, ANKRD50, EXOC6, MPP7
integral component of membrane	TMEFF2, TMEM132D, TMEM169, TMEM200A
dendrite development	FEZF2, OPA1, KLHL1
axon guidance	EPHA5, FEZF2, BDNF
glycoprotein metabolic process	ST6GAL2, XYLT1, GALNT14
transmembrane transport	KCNAB1, GRM7, SLC25A44
cell cycle	CCNY, CCNA1
synaptic vesicle membrane	ZNRF1
protein homo-oligomerization	KCTD4
RNA secondary structure unwinding	DDX10
uncharacterized	BEND4, C13orf36, DDX10, KIAA1239, LOC100287387, LOC157503

Genes were categorized according to GO processes, using David 6.8.

Supplementary Table S2 Maintenance of the EM/PM subtypes in the paired longitudinal glioma samples from CGGA.

Case ID	Sample ID	Pri/Rec Sample	sex	Age at Diagnosis (years)	Histological subtype[1]	WHO Grade	Tumor anatomical site[2]	Relative recurrence position[3]	PFS[4] (days)	OS[5] (days)	Censor[6]	IDH status	1p19q codel	7gain/10loss	EM/PM subtypes	RNA-seq	Tumor	Blood
PD013	CGGA_1124	Pri	Male	47	GBM	IV	Rt.T.	-	325	484	1	Wildtype	Non-codel	Combined_CNA	EM	Y	Y	-
	CGGA_1255	Rec			rGBM	IV	Rt.T.	L				Wildtype	Non-codel	Combined_CNA	EM	Y	Y	Y
PD015	CGGA_1758	Pri	Female	45	GBM	IV	Rt.P.	-	325	414	1	Wildtype	Non-codel	NA[7]	EM	Y	-	-
	CGGA_1865	Rec			rGBM	IV	Lt.T&P&O.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD021	CGGA_1749	Pri	Female	44	GBM	IV	Rt.F&P.	-	216	401	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1815	Rec			rGBM	IV	Rt.P&O.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD024	CGGA_604	Pri	Male	46	GBM	IV	Lt.O.	-	215	381	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_777	Rec			rGBM	IV	Lt.F&O.	D				Wildtype	Non-codel	NA	EM	Y	Y	-
PD026	CGGA_1227	Pri	Female	46	rGBM	IV	Rt.F.	-	433	1197	1	Wildtype	Non-codel	Combined_CNA	EM	Y	Y	Y
	CGGA_1492	Rec			rGBM	IV	Rt.F.	L				Wildtype	Non-codel	NA	EM	Y	-	-
PD033	CGGA_1177	Pri	Male	40	rGBM	IV	Rt.T&O.	-	358	449	1	Wildtype	Non-codel	NA	EM	Y	Y	-
	CGGA_1387	Rec			rGBM	IV	Rt.F&T&O.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD050	CGGA_1035	Pri	Female	60	GBM	IV	Lt.P&O.	-	252	567	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1078	Rec			rGBM	IV	Lt.P&O.	L				Wildtype	Non-codel	NA	EM	Y	Y	-
PD075	CGGA_1665	Pri	NA	NA	NA	NA	Rt.F.	-	358	NA	NA	NA	NA	NA	EM	Y	-	-
	CGGA_1772	Rec			NA	NA	Rt.T.	D				NA	NA	NA	EM	Y	-	-
PD102	CGGA_1410	Pri	Female	27	GBM	IV	Lt.F&P.	-	657	825	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1702	Rec			rGBM	IV	Lt.T.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD103	CGGA_1106	Pri	Male	37	GBM	IV	LRt.P&O.	-	259	420	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1208	Rec			rGBM	IV	LRt.P&O.	L				Wildtype	Non-codel	NA	EM	Y	-	-
PD112	CGGA_1459	Pri	Male	55	rAOA	III	Lt.T.	-	377	503	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1637	Rec			NA	NA	Lt.F&T.	D				NA	NA	NA	EM	Y	-	-
PD123	CGGA_1353	Pri	Male	65	GBM	IV	Rt.T&O.	-	677	1022	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1682	Rec			rGBM	IV	Rt.T.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD127	CGGA_1687	Rec	Male	14	GBM	IV	Rt.F.	-	NA	1738	0	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1911	Rec2			rGBM	IV	Lt.F.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD140	CGGA_1766	Pri	NA	NA	NA	NA	Rt.T&P.	-	257	NA	NA	NA	NA	NA	EM	Y	-	-
	CGGA_1853	Rec			NA	NA	Rt.T&P.	L				NA	Non-codel	Combined_CNA	EM	Y	Y	Y
PD004	CGGA_1232	Pri	Male	39	AOA	III	Lt.F.	-	1569	2067	1	Mutant	Non-codel	Combined_CNA	PM	Y	Y	Y
	CGGA_1915	Rec			NA	NA	Lt.F.	L				NA	NA	NA	PM	Y	-	-
PD005	CGGA_42	Pri	Male	38	A	II	Lt.F&T.	-	2611	2832	1	Mutant	Codel	NA	PM	Y	-	-
	CGGA_1519	Rec			NA	NA	Lt.F.	D				NA	NA	NA	PM	Y	-	-
PD011	CGGA_1169	Pri	Male	30	AOA	III	Rt.F.	-	877	1765	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_1632	Rec			NA	NA	Rt.T.	D				NA	Non-codel	NA	PM	Y	-	-
PD023	CGGA_1527	Pri	Male	47	AOA	III	Rt.F&T&P.	-	1608	1714	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_2124	Rec			NA	NA	Rt.T&P.	D				NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD027	CGGA_273	Pri	Female	35	OA	II	Lt.T.	-	2432	2635	1	Mutant	Non-codel	NA	PM	Y	Y	-
	CGGA_1609	Rec			NA	NA	Lt.T.	L				NA	NA	NA	PM	Y	Y	-

PD030	CGGA_D28	Pri	Male	25	AA	III	Lt.F&T.	-	510	860	1	Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
	CGGA_1170	Rec			sGBM	IV	Lt.F&T.	L				Mutant	Non-codel	NA	PM	Y	-	-
PD054	CGGA_1212	Pri	Male	31	AOA	III	Rt.F&T.	-	2186	2292	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_2123	Rec			NA	NA	Rt.F.	D				NA	NA	Combined_CNA	PM	Y	Y	Y
PD061	CGGA_482	Pri	Male	45	OA	III	Rt.F.	-	2157	2511	1	Mutant	Codel	NA	PM	Y	-	-
	CGGA_1628	Rec			NA	NA	Lt.F.	D				NA	NA	NA	PM	Y	-	-
PD062	CGGA_1219	Pri	Female	57	GBM	IV	Lt.T.	-	2010	2120	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_2062	Rec			rGBM	IV	NA	D				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD089	CGGA_1606	Pri	Female	28	AOA	III	Rt.F.	-	425	471	1	Wildtype	Non-codel	NA	PM	Y	-	-
	CGGA_1748	Rec			NA	NA	Lt.F&C.	D				NA	NA	NA	PM	Y	-	-
PD090	CGGA_314	Pri	Male	39	rAO	III	Lt.F.	-	1626	2568	1	Mutant	Codel	NA	PM	Y	-	-
	CGGA_1197	Rec			sGBM	IV	Rt.F&T.	D				Mutant	Codel	NA	PM	Y	-	-
PD096	CGGA_1969	Rec	NA	NA	NA	NA	Lt.F.	-	NA	NA	NA	NA	NA	No_combined_CNA	PM	Y	Y	Y
	CGGA_2017	Rec2			NA	NA	Lt.F.	L				NA	NA	No_combined_CNA	PM	Y	Y	
PD097	CGGA_1300	Pri	Male	35	AOA	III	Lt.F&P.	-	850	1793	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_1716	Rec			rAA	III	Rt.T&P&C.	D				Mutant	Non-codel	NA	PM	Y	-	-
PD100	CGGA_1403	Pri	Female	43	GBM	IV	Rt.F&P.	-	474	679	1	Wildtype	Non-codel	NA	PM	Y	-	-
	CGGA_1638	Rec			NA	NA	Rt.F&T&P.	D				NA	NA	NA	PM	Y	-	-
PD107	CGGA_680	Pri	Male	44	GBM	IV	Rt.F.	-	1852	2373	1	Wildtype	Non-codel	NA	PM	Y	-	-
	CGGA_P12	Rec			NA	NA	Rt.T.	D				NA	NA	NA	PM	Y	Y	-
PD114	CGGA_D04	Pri	Male	37	A	II	Lt.T.	-	2680	3359	0	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_P439	Rec			rA	II	Lt.T.	L				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD118	CGGA_705	Pri	Male	41	AA	III	Rt.F&T.	-	1432	1507	1	Mutant	Non-codel	No_combined_CNA	PM	Y	Y	-
	CGGA_1396	Rec			NA	NA	Rt.F&T.	L				NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD120	CGGA_1013	Pri	Female	38	A	II	Rt.T.	-	1441	1725	1	Mutant	Non-codel	No_combined_CNA	PM	Y	Y	-
	CGGA_1602	Rec			NA	NA	Rt.F&T&O.	D				NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD128	CGGA_1055	Pri	Male	43	AA	III	Lt.T.	-	1127	1611	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_1622	Rec			NA	NA	Lt.T.	D				NA	NA	NA	PM	Y	-	-
PD133	CGGA_1118	Pri	Male	31	rAA	III	Lt.F.	-	366	398	1	Mutant	Non-codel	No_combined_CNA	PM	Y	Y	-
	CGGA_1272	Rec			sGBM	IV	Lt.F.	L				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD136	CGGA_1103	Pri	Female	35	GBM	IV	Lt.F.	-	539	585	1	Mutant	Non-codel	No_combined_CNA	PM	Y	Y	-
	CGGA_1381	Rec			rGBM	IV	Lt.F&T.	D				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD058	CGGA_1547	Rec			NA	NA	Lt.T.	-				NA	NA	NA	PM	Y	-	-
	CGGA_2063	Rec2	NA	NA	NA	NA	Lt.P&O.	D	NA	NA	NA	NA	NA	NA	NL	Y	Y	-
	CGGA_2142	Rec3			NA	NA	Lt.T.	D				NA	NA	NA	PM	Y	Y	-
PD012	CGGA_1881	Pri	NA	NA	NA	NA	Lt.F&P.	-	446	NA	NA	NA	NA	NA	NL	Y	-	-
	CGGA_2103	Rec			NA	NA	Lt.F&T.	D				NA	Non-codel	Combined_CNA	EM	Y	Y	Y
PD017	CGGA_1024	Pri	Male	64	GBM	IV	Rt.F.	-	902	3074	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1337	Rec			rGBM	IV	LRt.F.	D				NA	Non-codel	NA	NL	Y	-	-
PD018	CGGA_139	Pri	Male	59	GBM	IV	Rt.P.	-	538	694	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_487	Rec			rGBM	IV	Rt.F&P.	D				Wildtype	Non-codel	NA	EM	Y	-	-
PD037	CGGA_1512	Pri	NA	NA	NA	NA	Lt.F.	-	536	NA	NA	NA	NA	NA	EM	Y	-	-
	CGGA_1719	Rec			NA	NA	Rt.F.	D				NA	NA	NA	NL	Y	-	-
PD049	CGGA_1214	Pri	Female	49	GBM	IV	Rt.F.	-	568	604	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1541	Rec			rGBM	IV	Lt.F&P&O.	D				Wildtype	Non-codel	NA	NL	Y	-	-

Patient	Sample	Type	Gender	Age	Histology	Grade	Location		N1	N2	N3	IDH	1p19q	CNA	Status			
PD081	CGGA_1049	Pri	Male	58	GBM	IV	Rt.T.	-	617	809	1	Wildtype	Non-codel	No_combined_CNA	EM	Y	Y	-
	CGGA_1257	Rec			rGBM	IV	Rt.T.	L				Wildtype	Non-codel	No_combined_CNA	NL	Y	Y	Y
PD099	CGGA_1114	Pri	Male	53	GBM	IV	Rt.Th.	-	322	460	1	Wildtype	Non-codel	NA	EM	Y	-	-
	CGGA_1248	Rec			rGBM	IV	Rt.T&Th.	D				Wildtype	Non-codel	NA	NL	Y	-	-
PD010	CGGA_2003	Rec	Male	40	rGBM	IV	Rt.F.	-	NA	827	0	Wildtype	Non-codel	No_combined_CNA	NL	Y	Y	Y
	CGGA_2082	Rec2			rGBM	IV	Lt.F.	D				Wildtype	Non-codel	No_combined_CNA	PM	Y	Y	-
PD029	CGGA_P356	Rec	Female	22	rOA	II	Rt.T.	-	351	569	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_P568	Rec2			rAOA	III	Rt.F&T.	D				Mutant	Codel	No_combined_CNA	PM	Y	Y	Y
PD031	CGGA_634	Pri	Female	35	AOA	III	Rt.P&O.	-	1882	2633	1	Mutant	Codel	No_combined_CNA	NL	Y	Y	-
	CGGA_1585	Rec			NA	NA	Rt.P.	D				NA	Codel	No_combined_CNA	PM	Y	Y	Y
PD034	CGGA_1018	Rec	Male	50	rO	II	Rt.F&T.	-	1394	2527	1	Mutant	Codel	NA	PM	Y	Y	-
	CGGA_1591	Rec2			rAOA	III	Rt.F&T.	L				Mutant	Non-codel	NA	NL	Y	Y	-
PD035	CGGA_320	Pri	Male	31	OA	II	Rt.F&T.	-	2048	3005	1	Mutant	Codel	NA	NL	Y	Y	-
	CGGA_1450	Rec			sGBM	IV	Rt.F.	D				Mutant	Codel	NA	PM	Y	-	-
PD038	CGGA_112	Pri	Male	17	OA	II	Lt.F&T.	-	983	1534	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_810	Rec			rAO	III	Lt.F&T.	L				Mutant	Non-codel	NA	NL	Y	Y	-
PD043	CGGA_1113	Pri	Male	34	AOA	III	Rt.F.	-	1154	1265	1	Mutant	Codel	NA	PM	Y	-	-
	CGGA_1676	Rec			NA	NA	Rt.F&P.	D				NA	NA	NA	NL	Y	-	-
PD051	CGGA_1525	Pri	Male	41	AOA	III	Rt.F&P.	-	1435	1686	1	NA	Non-codel	NA	NL	Y	-	-
	CGGA_2046	Rec			rAA	III	LRt.P.	D				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD053	CGGA_400	Rec	Female	38	rAA	III	Rt.F.	-	596	1321	1	Mutant	Non-codel	NA	NL	Y	Y	-
	CGGA_867	Rec2			rAA	III	Rt.F.	L				Mutant	Non-codel	NA	PM	Y	Y	-
PD064	CGGA_685	Pri	Female	20	A	II	Lt.F&T.	-	3073	3239	1	Mutant	Non-codel	NA	PM	Y	-	-
	CGGA_P375	Rec			NA	NA	Lt.F&T.	L				NA	NA	NA	NL	Y	-	-
PD065	CGGA_1973	Pri	NA	NA	NA	NA	Rt.F&T&P.	-	335	NA	NA	NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
	CGGA_2093	Rec			NA	NA	Rt.F&T&P.	L				NA	Non-codel	No_combined_CNA	NL	Y	Y	Y
PD067	CGGA_1592	Rec	Male	37	rAOA	III	Rt.F.	-	NA	1588	1	Mutant	Codel	No_combined_CNA	PM	Y	Y	Y
	CGGA_1771	Rec2			rAOA	III	Rt.F.	L				Mutant	Non-codel	NA	NL	Y	-	-
PD076	CGGA_721	Pri	Male	45	OA	II	Lt.F.	-	1856	2552	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_1625	Rec			NA	NA	Lt.T.	D				NA	NA	NA	PM	Y	-	-
PD078	CGGA_503	Pri	Male	51	OA	II	Lt.T.	-	3004	4084	0	Mutant	Non-codel	No_combined_CNA	NL	Y	Y	-
	CGGA_1925	Rec			NA	NA	Lt.F&T.	D				NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD092	CGGA_1356	Rec	Male	52	rAOA	III	Lt.F&P.	-	674	948	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_1683	Rec2			NA	NA	Lt.F&P.	L				NA	NA	NA	PM	Y	-	-
PD098	CGGA_583	Pri	Female	36	A	II	Rt.T.	-	2806	3107	1	Mutant	NA	NA	NL	Y	-	-
	CGGA_P152	Rec			NA	NA	Rt.T.	L				NA	NA	NA	PM	Y	-	-
PD125	CGGA_882	Rec	Male	30	rAOA	III	Lt.F.	-	1527	1008	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_1554	Rec2			rAOA	III	Lt.F&P.	D				Mutant	Codel	NA	PM	Y	-	-
PD145	CGGA_P316	Rec	Male	44	rA	II	Rt.F.	-	240	567	0	NA	Non-codel	NA	NL	Y	-	-
	CGGA_P459	Rec2			NA	NA	Rt.F.	L				NA	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD008	CGGA_1148	Pri	Male	37	A	II	Rt.F&P.	-	457	596	1	Mutant	Non-codel	NA	unidentified	Y	-	-
	CGGA_1394	Rec			rGBM	IV	Rt.F&T&P.	D				Mutant	Non-codel	No_combined_CNA	PM	Y	Y	Y
PD016	CGGA_337	Pri	Female	50	AOA	III	LRt.F.	-	565	1008	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_773	Rec			sGBM	IV	LRt.F.	L				Mutant	Non-codel	NA	NL	Y	-	-

Patient	Sample	Type	Gender	Age	Histology	Grade	Location	Rec	PFS	OS	Status	IDH	1p19q	CNA				
PD044	CGGA_1861	Pri	NA	NA	NA	NA	Rt.F&T.	-	232	NA	NA	NA	Non-codel	No_combined_CNA	NL	Y	Y	Y
	CGGA_1940	Rec			NA	NA	NA	D				NA	NA	NA	NL	Y	-	-
PD048	CGGA_707	Pri	Female	39	OA	III	Lt.F.	-	2788	3299	1	Mutant	Codel	NA	NL	Y	Y	-
	CGGA_P269	Rec			rAO	III	Lt.F&P.	D				Wildtype	Codel	NA	NL	Y	-	-
PD063	CGGA_1776	Rec	Male	23	rGBM	IV	Lt.P.	-	188	259	1	Wildtype	Non-codel	NA	NL	Y	-	-
	CGGA_P106	Rec2			rGBM	IV	Lt.T&P.	D				Wildtype	Non-codel	NA	NL	Y	-	-
PD117	CGGA_1935	Pri	NA	NA	NA	NA	Rt.F.	-	209	NA	NA	NA	NA	NA	NL	Y	-	-
	CGGA_2004	Rec			NA	NA	Rt.F.	L				NA	NA	NA	NL	Y	Y	-
PD138	CGGA_1487	Rec	Female	49	rAA	III	Lt.F.	-	469	520	1	Wildtype	Non-codel	NA	NL	Y	-	-
	CGGA_1688	Rec2			rAA	III	Lt.F.	L				Wildtype	Non-codel	NA	NL	Y	-	-
PD139	CGGA_1508	Pri	Male	39	AOA	III	Lt.F.	-	1800	1049	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_2149	Rec			NA	NA	LRt.F&T.	D				NA	NA	NA	NL	Y	Y	-
PD146	CGGA_P364	Pri	Female	41	rAA	III	Lt.F.	-	305	495	1	Mutant	Non-codel	NA	NL	Y	-	-
	CGGA_P541	Rec			NA	NA	Lt.F&T.	D				NA	Non-codel	No_combined_CNA	NL	Y	Y	Y

[1] A, astrocytoma; O, oligodendroglioma; OA, oligoastrocytoma; AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; AOA, anaplastic oligoastrocytoma; GBM, glioblastoma; sGBM, secondary glioblastoma; NA, Not avaliable; r recurrent.

[2] Lt., Left hemisphere; Rt., Right hemisphere; F., Frontal lobe; T., Temporal lobe; P., Parietal lobe; O., Occipital lobe;C., Cerecellar region; Th.,Thalamic region.

[3] D, distant recurrence; L, local recurrence. Local recurrence indicates gliomas recurred at the same site of the initial tumor; distant recurrence indicates gliomas recurred at a different anatomical site of the brain, including in the other hemisphere relative to the initial tumor site.

[4] PFS, progression free survival, corresponding to the interval between the initial surgery and the surgery at the first recurrence.

[5] OS, overall survival

[6] 0, alive; 1, dead.

[7]NA, not available.

Supplementary Table S3 Maintenance of the EM/PM subtypes in previously reported longitudinal cohorts.

Data set	Platform	Case ID	Sample ID	Pri/Rec Sample	Sex	Age at the first diagnosis (years)	Histological subtype[1]	WHO Grade	Surgical Intervals (weeks)	Survival (weeks)	Censor	*IDH* status	1p/19q co-del	7gain/10loss	EM/PM subtype
TCGA database	RNA sequencing	TCGA-06-0125	TCGA-06-0125-01A-01R-1849-01	Primary	F	63	GBM		114	204	1	WT	Non-Codel	No combined CNA	EM
			TCGA-06-0125-02A-11R-2005-01	Secondary											EM
		TCGA-06-0190	TCGA-06-0190-01A-01R-1849-01	Primary	M	62	GBM		13	45	1	WT	Non-Codel	7 gain/10 loss	EM
			TCGA-06-0190-02A-01R-2005-01	Secondary											EM
		TCGA-06-0210	TCGA-06-0210-01A-01R-1849-01	Primary	F	72	GBM		10	32	1	WT	Non-Codel	7 gain/10 loss	EM
			TCGA-06-0210-02A-01R-2005-01	Secondary											EM
		TCGA-06-0211	TCGA-06-0211-01A-01R-1849-01	Primary	M	47	GBM	IV	8	51	1	WT	Non-Codel	7 gain/10 loss	EM
			TCGA-06-0211-01B-01R-1849-01	Primary											EM
			TCGA-06-0211-02A-02R-2005-01	Secondary											EM
		TCGA-14-1034	TCGA-14-1034-01A-01R-1849-01	Primary	F	60	GBM		39	68	1	WT	Non-Codel	7 gain/10 loss	EM
			TCGA-14-1034-02B-01R-2005-01	Secondary											EM
		TCGA-19-4065	TCGA-19-4065-01A-01R-2005-01	Primary	M	36	GBM		10	30	0	NA	Non-Codel	7 gain/10 loss	EM
			TCGA-19-4065-02A-11R-2005-01	Secondary											EM
		TCGA-FG-5963	TCGA-FG-5963-01A-11R-1708-07	Primary	M	23	Ast.	Ⅲ	NA	109	1	WT	Non-Codel	No combined CNA	EM
			TCGA-FG-5963-02A-12R-A29R-07	Secondary			NA	NA							EM
		TCGA-DU-6404	TCGA-DU-6404-01A-11R-1708-07	Primary	F	24	Oligo.	Ⅲ	NA	573	1	WT	Non-Codel	No combined CNA	EM
			TCGA-DU-6404-02A-21R-A36H-07	Secondary			NA	NA							EM
			TCGA-DU-6404-02B-11R-A36H-07	Secondary											EM
		TCGA-FG-5965	TCGA-FG-5965-01B-11R-1896-07	Primary	F	39	Oligo.	Ⅱ	NA	158	1	Mut	Non-Codel	No combined CNA	PM
			TCGA-FG-5965-02A-11R-A29R-07	Secondary			NA	NA							PM
			TCGA-FG-5965-02B-11R-A29R-07	Secondary											PM
		TCGA-DH-A669	TCGA-DH-A669-01A-12R-A31N-07	Primary	M	70	Oligo.	Ⅲ	NA	129	1	Mut	Codel	No combined CNA	PM
			TCGA-DH-A669-02A-11R-A31N-07	Secondary			NA	NA							PM
		TCGA-DU-5870	TCGA-DU-5870-01A-11R-1708-07	Primary	F	34	Oligo.	Ⅱ	NA	781	0	Mut	Codel	No combined CNA	PM
			TCGA-DU-5870-02A-12R-A36H-07	Secondary			NA	NA							PM
		TCGA-DU-6397	TCGA-DU-6397-01A-11R-1708-07	Primary	M	45	Oligo.	Ⅲ	NA	197	1	Mut	Codel	No combined CNA	PM
			TCGA-DU-6397-02A-12R-A36H-07	Secondary			NA	NA							PM
		TCGA-DU-6407	TCGA-DU-6407-01A-13R-1708-07	Primary	F	35	Oligo.	Ⅱ	NA	405	1	Mut	Non-Codel	No combined CNA	PM
			TCGA-DU-6407-02A-12R-A36H-07	Secondary			NA	NA							PM
			TCGA-DU-6407-02B-11R-A36H-07	Secondary											PM
		TCGA-DU-7304	TCGA-DU-7304-01A-12R-2090-07	Primary	M	43	Oligo.	Ⅲ	NA	100	1	Mut	Non-Codel	No combined CNA	PM
			TCGA-DU-7304-02A-12R-A36H-07	Secondary			NA	NA							PM
		TCGA-TQ-A7RK	TCGA-TQ-A7RK-01A-11R-A33Z-07	Primary	NA	NA	NA	NA	NA	NA	NA	Mut	Non-Codel	No combined CNA	PM
			TCGA-TQ-A7RK-02A-11R-A36H-07	Secondary											PM
			TCGA-TQ-A7RK-02B-11R-A40A-07	Secondary											PM
		TCGA-TQ-A8XE	TCGA-TQ-A8XE-01A-11R-A36H-07	Primary	NA	NA	NA	NA	NA	NA	NA	Mut	Non-Codel	No combined CNA	PM
			TCGA-TQ-A8XE-02A-11R-A36H-07	Secondary											PM
		TCGA-TQ-A7RV	TCGA-TQ-A7RV-01A-21R-A34F-07	Primary	NA	NA	NA	NA	NA	NA	NA	Mut	Non-Codel	No combined CNA	PM
			TCGA-TQ-A7RV-02A-11R-A36H-07	Secondary											NL
		TCGA-TM-A7CF	TCGA-TM-A7CF-01A-11R-A32Q-07	Primary	F	41	Ast.	Ⅱ	NA	207	0	Mut	Non-Codel	No combined CNA	NL
			TCGA-TM-A7CF-02A-11R-A32Q-07	Secondary			NA	NA							PM
		TCGA-FG-A4MT	TCGA-FG-A4MT-01A-11R-A26U-07	Primary	F	27	Oligo.	Ⅱ	NA	164	0	Mut	Non-Codel	No combined CNA	PM
			TCGA-FG-A4MT-02A-11R-A29R-07	Secondary			NA	NA							NL

		TCGA-DU-5872	TCGA-DU-5872-01A-11R-1708-07	Primary	F	43	Oligo.	Ⅱ	NA	75	0	Mut	Non-Codel	No combined CNA	PM
			TCGA-DU-5872-02A-21R-A36H-07	Secondary			NA	NA							unidentified
SRP074425	RNA sequencing	R001	R001.I	Primary	M	70	GBM	IV	22	28	0	WT	Non-Codel	NA	EM
			R001.R	Secondary											EM
		R002	R002.I	Primary	M	42			43	76	0	WT	Non-Codel	NA	EM
			R002.R	Secondary											EM
		R004	R004.I	Primary	F	50			25	117	0	WT	Non-Codel	NA	EM
			R004.R	Secondary											EM
		R005	R005.I	Primary	F	58			22	55	0	WT	Non-Codel	NA	EM
			R005.R	Secondary											EM
		R007	R007.I	Primary	M	69			49	91	0	WT	Non-Codel	NA	EM
			R007.R*	Secondary											EM
		R008	R008.I	Primary	F	46			43	65	0	WT	Non-Codel	NA	EM
			R008.R	Secondary											EM
		R009	R009.I	Primary	F	67			172	199	0	Mut	Non-Codel	NA	PM
			R009.R	Secondary											PM
		R010	R010.I	Primary	M	50			71	98	0	WT	Non-Codel	NA	PM
			R010.R*	Secondary								Mut			PM
		R012	R012.I	Primary	M	49			137	194	0	Mut	Non-Codel	NA	PM
			R012.R	Secondary											PM
		R003	R003.I	Primary	M	67			37	73	0	WT	Non-Codel	NA	EM
			R003.R	Secondary											NL
		R006	R006.I	Primary	M	59			48	75	0	WT	Non-Codel	NA	NL
			R006.R	Secondary											EM
		R019	R019.I	Primary	M	48			37	79	0	WT	Non-Codel	NA	EM
			R019.R	Secondary											NL
		R056	R056.I	Primary	F	42			103	260	1	WT	Non-Codel	NA	EM
			R056.R	Secondary											EM
		R059	R059.I	Primary	F	37			81	209	1	WT	Non-Codel	NA	EM
			R059.R	Secondary											EM
		R060	R060.I	Primary	M	32			61	166	1	WT	Non-Codel	NA	EM
			R060.R	Secondary											EM
		R061	R061.I	Primary	M	48			10	149	0	WT	Non-Codel	NA	EM
			R061.R	Secondary											EM
		R063	R063.I	Primary	F	34			127	140	1	WT	Non-Codel	NA	EM
			R063.R	Secondary											EM
		R064	R064.I	Primary	F	56			38	181	1	WT	Non-Codel	NA	EM
			R064.R	Secondary											EM
		R066	R066.I	Primary	M	51			61	100	1	WT	Non-Codel	NA	EM
			R066.R	Secondary											EM
		R067	R067.I	Primary	M	51			28	94	0	WT	Non-Codel	NA	EM
			R067.R	Secondary											EM
		R068	R068.I	Primary	M	74			67	82	0	WT	Non-Codel	NA	EM
			R068.R	Secondary											EM
		R072	R072.I	Primary	M	74			23	59	0	WT	Non-Codel	NA	EM
			R072.R	Secondary											EM
		R074	R074.I	Primary	M	z	GBM	IV	29	51	0	WT	Non-Codel	NA	EM
			R074.R	Secondary											EM
		R081	R081.I	Primary	F	58			31	72	0	NA	Non-Codel	NA	EM

Study	Platform	Patient	Sample	Type	Sex	Age	Histology	Grade				IDH	Codel		Class
		R081	R081.R	Secondary	F	38			31	72	0	NA	Non-Codel	NA	EM
EGAS0000 1001041	Illumina HiSeq 2000	R082	R082.I	Primary	M	49			11	46	1	NA	Non-Codel	NA	EM
			R082.R	Secondary											EM
		R083	R083.I	Primary	M	50			68	145	0	NA	Non-Codel	NA	EM
			R083.R	Secondary											EM
		R085	R085.I	Primary	M	51			55	138	0	NA	Non-Codel	NA	EM
			R085.R	Secondary											EM
		R088	R088.I	Primary	F	32			50	107	0	NA	Non-Codel	NA	EM
			R088.R*	Secondary											EM
		R090	R090.I	Primary	M	44			22	55	0	NA	Non-Codel	NA	EM
			R090.R	Secondary											EM
		R076	R076.I	Primary	M	40			11	247	0	Mut	Non-Codel	NA	PM
			R076.R	Secondary											PM
		R077	R077.I	Primary	M	44			68	191	1	Mut	Non-Codel	NA	PM
			R077.R*	Secondary											PM
		R084	R084.I	Primary	F	43			88	142	0	NA	Non-Codel	NA	PM
			R084.R*	Secondary											PM
		R070	R070.I	Primary	F	72			29	71	1	WT	Non-Codel	NA	PM
			R070.R	Secondary											PM
		R071	R071.I	Primary	M	65			47	67	0	WT	Non-Codel	NA	EM
			R071.R	Secondary											NL
		R065	R065.I	Primary	F	38			64	111	0	WT	Non-Codel	NA	EM
			R065.R	Secondary											NL
		R089	R089.I	Primary	M	41	GBM	IV	15	65	0	NA	Non-Codel	NA	EM
			R089.R	Secondary											NL
		R091	R091.I	Primary	M	45			29	51	0	NA	Non-Codel	NA	EM
			R091.R	Secondary											NL
		R092	R092.I	Primary	F	47			26	47	0	NA	Non-Codel	NA	EM
			R092.R	Secondary											NL
		R093	R093.I	Primary	M	73			32	36	1	NA	Non-Codel	NA	EM
			R093.R	Secondary											NL
		R080	R080.I	Primary	M	60			87	142	0	NA	Non-Codel	NA	PM
			R080.R*	Secondary			GBM	IV							NL
		R086	R086.I	Primary	M	29			83	135	0	NA	Non-Codel	NA	PM
			R086.R	Secondary											NL
		R078	R078.I	Primary	M	39			123	349	0	NA	Non-Codel	NA	EM
			R078.R	Secondary			GBM	IV							PM
		R087	R087.I	Primary	F	37			79	118	1	NA	Non-Codel	NA	EM
			R087.R	Secondary											PM
		R095	R095.I	Primary	NA	61			39	85	1	WT	Non-Codel	NA	EM
			R095.R	Secondary											EM
		R099	R099.I	Primary	NA	57			13	83	1	WT	Non-Codel	NA	EM
			R099.R	Secondary											EM
		R100	R100.I	Primary	NA	45			20	76	0	WT	Non-Codel	NA	EM
			R100.R	Secondary											EM
		R101	R101.I	Primary	NA	63			12	60	0	WT	Non-Codel	NA	EM
			R101.R	Secondary											EM
		R102	R102.I	Primary	NA	69			44	70	0	NA	Non-Codel	NA	EM

EGAS0000 1001800	Illumina HiSeq 2500 , whole-exome sequencing, RNA sequencing	R102	R102.R	Secondary	NA	69			44	70	0	NA	Non-Codel	NA	EM
		R106	R106.I	Primary	NA	51	GBM	IV	41	57	0	WT	Non-Codel	NA	EM
			R106.R	Secondary											EM
		R107	R107.I	Primary	NA	52			30	68	1	WT	Non-Codel	NA	EM
			R107.R	Secondary											EM
		R108	R108.I	Primary	NA	56			21	37	1	WT	Non-Codel	NA	EM
			R108.R	Secondary											EM
		R109	R109.I	Primary	NA	51			50	80	0	WT	Non-Codel	NA	EM
			R109.R	Secondary											EM
		R110	R110.I	Primary	NA	49			10	35	1	WT	Non-Codel	NA	EM
			R110.R	Secondary											EM
		R112	R112.I	Primary	NA	70			6	44	0	NA	Non-Codel	NA	EM
			R112.R	Secondary											EM
		R113	R113.I	Primary	NA	51			13	79	0	NA	Non-Codel	NA	EM
			R113.R	Secondary											EM
		R114	R114.I	Primary	NA	45	GBM	IV	37	320	1	NA	Non-Codel	NA	PM
			R114.R	Secondary											PM
		R111	R111.I	Primary	NA	31	GBM	IV	27	61	0	NA	Non-Codel	NA	EM
			R111.R	Secondary											NL
		R104	R104.I	Primary	NA	54	GBM	IV	49	118	1	WT	Non-Codel	NA	EM
			R104.R	Secondary											NL
		R103	R103.I	Primary	NA	55	GBM	IV	14	80	0	WT	Non-Codel	NA	PM
			R103.R	Secondary											EM
GSE4271	Affymetrix Human Genome U133A/B Array	3781	PRB3781	Primary	43	43	GBM		NA	210	1	NA	19 no change	No combined CNA	EM
			PRB3755	Secondary			GBM						NA	NA	EM
		3746	PRB3746	Primary	43	43	GBM		NA	313	0	NA	19 gain	7 gain/10 loss	EM
			PRB3785	Secondary			GBM						NA	NA	EM
		4094	PRB4094	Primary	32	32	GBM		NA	51	0	NA	19 no change	7 gain/10 loss	EM
			PRB4095	Secondary			GBM						19 no change	7 gain/10 loss	EM
		4128	PRB4128	Primary	57	57	GBM		NA	70	0	NA	NA	NA	EM
			PRB4096	Secondary			GBM						NA	NA	EM
		4097	PRB4097	Primary	57	57	GBM	IV	NA	62	0	NA	19 gain	7 gain/10 loss	EM
			PRB4098	Secondary			GBM						NA	NA	EM
		4102	PRB4102	Primary	68	68	GBM		NA	91	0	NA	NA	NA	EM
			PRB4103	Secondary			GBM						NA	NA	EM
		4127	PRB4127	Primary	72	72	GBM		NA	57	0	NA	NA	NA	EM
			PRB4123	Secondary			GBM						19 loss	7 gain/10 loss	EM
		4122	PRB4122	Primary	72	72	GBM		NA	65	0	NA	19 no change	No combined CNA	EM
			PRB4124	Secondary			GBM						NA	NA	EM
		4767	PRB4767	Primary	44	44	GBM		NA	174	0	NA	NA	NA	PM
			PRB4756	Secondary			GBM						19 no change	No combined CNA	PM
		4780	PRB4780	Primary	32	32	Ast.	III	NA	244	0	NA	NA	NA	PM
			PRB4761	Secondary			GBM	IV					19 no change	No combined CNA	PM
		4785	PRB4785	Primary	54	54	GBM	IV	NA	53	0	NA	NA	NA	PM
			PRB4771	Secondary			GBM	IV					NA	NA	PM
		4779	PRB4779	Primary	34	34	Ast.	III	NA	108	0	NA	NA	NA	PM
			PRB4773	Secondary			Ast.	III					NA	NA	PM
		4778	PRB4778	Primary	23	23	Ast.	III	NA	115	0	NA	19 no change	No combined CNA	PM

		ID	Sample	Type			Tumor	Grade					chr19	CNA	Class
		4778	PRB4777	Secondary	25	25	GBM	IV	NA	115	0	NA	19 no change	No combined CNA	PM
		4755	PRB4755	Primary	25	25	Ast.	III	NA	175	1	NA	NA	NA	PM
			PRB4790	Secondary			Ast.	III					NA	NA	PM
		4782	PRB4782	Primary	49	49	GBM	IV	NA	73	0	NA	NA	NA	PM
			PRB4791	Secondary			GBM	IV					NA	NA	PM
		3758	PRB3758	Primary	34	34	GBM	IV	NA	203	0	NA	19 loss	No combined CNA	PM
			PRB3751	Secondary			GBM	IV					19 loss	No combined CNA	PM
		3744	PRB3744	Primary	60	60	GBM	IV	NA	131	0	NA	19 no change	7 gain/10 loss	PM
			PRB3777	Secondary			GBM	IV					19 no change	7 gain/10 loss	PM
		3906	PRB3906	Primary	32	32	GBM	IV	NA	39	0	NA	19 loss	7 gain/10 loss	PM
			PRB3840	Secondary			GBM	IV					19 no change	No combined CNA	PM
		4759	PRB4759	Primary	43	43	Ast.	III	NA	47	0	NA	NA	NA	EM
			PRB4746	Secondary			Ast.	III					NA	NA	NL
		3774	PRB3774	Primary	48	48	GBM	IV	NA	97	0	NA	19 no change	7 gain/10 loss	NL
			PRB3752	Secondary			GBM	IV					NA	NA	NL
		9907	PRB9907	Primary	25	25	GBM	IV	NA	146	1	NA	19 no change	No combined CNA	NL
			PRB9938	Secondary			GBM	IV					19 no change	No combined CNA	NL
		3748	PRB3748	Primary	45	45	GBM	IV	NA	70	0	NA	19 loss	No combined CNA	PM
			PRB3780	Secondary			GBM	IV					19 loss	No combined CNA	EM
		4783	PRB4783	Primary	45	45	Ast.	III	NA	46	0	NA	NA	NA	PM
			PRB4776	Secondary			GBM	IV					19 no change	7 gain/10 loss	EM
GSE62153	Illumina HumanHT-12 V4.0 expression beadchip	003	GBM003	Primary	M	33	GBM	IV	NA	NA	NA	NA	NA	NA	EM
			GBM009	Secondary											EM
		006	GBM006	Primary	M	66			NA	NA	NA	NA	NA	NA	EM
			GBM012	Secondary											EM
		007	GBM007	Primary	M	52			NA	NA	NA	NA	NA	NA	EM
			GBM029	Secondary											EM
		030	GBM030	Primary	F	53	GBM	IV	NA	NA	NA	NA	NA	NA	EM
			GBM031	Secondary											EM
		038	GBM038	Primary	M	68			NA	NA	NA	NA	NA	NA	EM
			GBM039	Secondary											EM
		044	GBM044	Primary	F	36			NA	NA	NA	NA	NA	NA	EM
			GBM050	Secondary											EM
		023	GBM023	Primary	F	55			NA	NA	NA	NA	NA	NA	PM
			GBM028	Secondary											PM
		042	GBM042	Primary	M	72	GBM	IV	NA	NA	NA	NA	NA	NA	PM
			GBM048	Secondary											PM
		046	GBM046	Primary	F	72			NA	NA	NA	NA	NA	NA	PM
			GBM052	Secondary											PM
		004	GBM004	Primary	F	33	GBM	IV	NA	NA	NA	NA	NA	NA	NL
			GBM010	Secondary											EM
		045	GBM045	Primary	M	45			NA	NA	NA	NA	NA	NA	EM
			GBM051	Secondary											NL
		022	GBM022	Primary	M	35			NA	NA	NA	NA	NA	NA	PM
			GBM027	Secondary											EM
		034	GBM034	Primary	M	55			NA	NA	NA	NA	NA	NA	EM
			GBM035	Secondary		GBM	IV								PM

GSE	Platform	Patient	Sample	Type	Sex	Age	Diagnosis[1]	Grade							
		036	GBM036	Primary	F	60	GBM	IV	NA	NA	NA	NA	NA	NA	PM
			GBM037	Secondary											EM
		043	GBM043	Primary	F	35			NA	NA	NA	NA	NA	NA	EM
			GBM049	Secondary											PM
GSE42669	Affymetrix Human Gene 1.0 ST Array [transcript (gene) version]	07-437	PC-NS07-437	Primary	F	58	GBM	IV	NA	71	1	NA	NA	NA	EM
			PC-NS08-559	Secondary											EM
		07-458	PC-NS07-458	Primary	M	51			NA	149	1	NA	NA	NA	EM
			PC-NS08-594	Secondary											EM
		08-538	PC-NS08-538	Primary	F	37			NA	195	0	NA	NA	NA	EM
			PC-NS09-773	Secondary											EM
		08-567	PC-NS08-567	Primary	F	65	GBM	IV	NA	NA	1	NA	NA	NA	EM
			PC-NS09-732	Secondary											EM
		08-577	PC-NS08-577	Primary	F	62			NA	45	1	NA	NA	NA	EM
			PC-NS09-680	Secondary											EM
		08-592	PC-NS08-592	Primary	M	44			NA	64	1	NA	NA	NA	EM
			PC-NS09-660	Secondary											EM
		09-780	PC-NS09-780	Primary	M	74			NA	65	1	NA	NA	NA	EM
			IRCR-GBM10-025	Secondary											EM
		08-586	PC-NS08-586	Primary	M	40	GBM	IV	NA	28	1	NA	NA	NA	PM
			PC-NS09-647	Secondary											PM
		07-460	PC-NS07-460	Primary	F	32			NA	110	1	NA	NA	NA	EM
			PC-NS08-568	Secondary											NL
		08-585	PC-NS08-585	Primary	M	22	GBM	IV	NA	123	1	NA	NA	NA	NL
			PC-NS09-663	Secondary											EM
		09-672	PC-NS09-672	Primary	M	51			NA	NA	0	NA	NA	NA	NL
			PC-NS09-723	Secondary											EM
		09-671	PC-NS09-671	Primary	F	47	GBM	IV	NA	48	1	NA	NA	NA	PM
			PC-NS09-740	Secondary											NL

[1] Ast., astrocytoma; Oligo., oligodendroglioma; GBM, glioblastoma; NA, Not avaliable.

*: hypermutated samples (Wang et al., Nature Genetics 48:768-776, 2016).

Supplementary Table S4 Clinical information, canonical genomic alterations and EM/PM subtyping results in multi-regionally sampled gliomas analyzed in this study.

Data Resource	Patient ID	Gender	Age	Histology[1]	CNV	RNA-seq site	No. of Samples EM/PM Subtyped*	IDH1 mutation	IDH2 mutation	ATRX mutation	TP53 mutation	EM/PM subtype
Yang et al. Aging, 2019	NO.01	M	62	rGBM	No typical CNA	3	3	ND	yes	ND	yes	EM
	NO.04	M	66	GBM	7 gain/10 loss	3	3	ND	ND	ND	ND	EM
	NO.05-R	M	46	rGBM	No typical CNA	4	4	ND	ND	ND	ND	EM
	NO.09	M	70	GBM	7 gain/10 loss	5	5	ND	ND	ND	ND	EM
	NO.12	M	60	GBM	7 gain/10 loss	6	6	ND	ND	ND	ND	EM
	NO.13	F	36	Oligo.	1p/19q codel	7	7	yes	ND	ND	ND	PM
	NO.14	F	67	GBM	7 gain/10 loss	7	7	ND	ND	ND	ND	EM
	NO.15	M	78	Ast.	7 gain/10 loss	6	6	ND	ND	ND	ND	EM
	NO.16	F	36	Ast.	No typical CNA	6	6	yes	ND	yes	ND	PM
	NO.17	M	46	GBM	7 gain/10 loss	6	5	ND	ND	ND	ND	EM
	NO.18	M	60	GBM	7 gain/10 loss	4	2	ND	ND	yes	yes	EM
	NO.19	M	54	GBM	7 gain/10 loss	6	6	ND	ND	yes	yes	EM
IVY GAP	W1	M	67	GBM	7gain/10loss	7	7	ND	ND	ND	yes	EM
	W2	F	65	GBM	7gain/10loss	10	10	ND	ND	ND	ND	EM
	W3	F	66	GBM	7gain/10loss	6	6	ND	yes	ND	ND	EM
	W4	F	51	GBM	No typical CNA	6	6	yes (R314I)	ND	yes	yes	EM
	W5	F	65	GBM	10loss	8	8	ND	ND	ND	ND	EM
	W6	F	73	GBM	No typical CNA	2	2	ND	ND	ND	ND	EM
	W7	M	61	GBM	7gain/10loss	3	3	ND	ND	yes	ND	EM
	W8	F	50	GBM	10loss	7	7	ND	ND	ND	ND	EM
	W9	M	51	GBM	7gain/10loss	5	5	ND	ND	ND	ND	EM
	W10	F	45	GBM	1p19q codel	6	6	yes	ND	ND	yes	PM
	W11	M	58	GBM	No typical CNA	10	10	ND	ND	ND	ND	EM
	W12	F	61	GBM	7gain/10loss	4	4	ND	ND	ND	ND	EM
	W13	F	60	GBM	No typical CNA	3	3	ND	ND	ND	ND	EM
	W16	M	77	GBM	7gain/10loss	5	5	ND	ND	ND	ND	EM
	W20	M	44	GBM	No typical CNA	6	6	ND	ND	ND	ND	EM
	W21	F	55	GBM	7gain/10loss	4	4	ND	ND	ND	ND	EM
	W22	F	53	GBM	7gain/10loss	7	7	ND	ND	ND	ND	EM
	W26	F	58	GBM	10loss	7	7	ND	ND	ND	ND	EM
	W27	M	65	GBM	NA	5	5	ND	ND	ND	ND	EM
	W28	M	69	GBM	NA	4	0	ND	ND	ND	ND	unidentified
	W29	M	74	GBM	10loss	6	6	ND	ND	ND	ND	EM
	W31	M	18	GBM	1p19q codel	9	9	yes	ND	yes	yes	PM
	W32	M	57	GBM	7gain	5	5	ND	ND	ND	ND	PM
	W33	M	61	GBM	7gain	4	4	ND	ND	ND	ND	EM
	W34	M	74	GBM	7gain/10loss	6	6	ND	ND	ND	ND	EM
	W36	M	62	GBM	No typical CNA	2	2	ND	ND	ND	ND	EM
	W38	F	65	GBM	7gain/10loss	3	3	ND	ND	ND	yes	EM
	W39	F	68	GBM	10loss	2	2	ND	ND	ND	ND	EM
	W40	M	65	GBM	7gain/10loss	4	4	ND	ND	yes	yes	EM
	W42	F	60	GBM	No typical CNA	4	4	ND	ND	ND	yes	EM(3), PM(1)
	W43	F	62	GBM	10loss	4	4	ND	ND	ND	ND	EM
	W48	M	52	GBM	10loss	2	2	ND	ND	ND	ND	EM
	W53	M	55	GBM	7gain/10loss	9	9	ND	yes	ND	yes	EM
	W54	M	58	GBM	No typical CNA	4	4	ND	ND	ND	ND	PM
	W55	M	53	GBM	10loss	10	10	ND	ND	ND	ND	EM
TCGA	TCGA-06-0211	M	47	GBM	7gain/10loss	2	2	ND	ND	ND	ND	EM
	TCGA-DU-6404	F	24	Oligo.	7gain	2	2	ND	ND	yes	ND	EM
	TCGA-DU-6407	F	35	Oligo.	No typical CNA	2	2	yes	ND	yes	yes	PM
	TCGA-TQ-A7RK	NA	28	OA.	No typical CNA	2	2	yes	ND	yes	yes	PM
	TCGA-FG-5965	M	61	Oligo.	1p/19q codel	2	2	yes	ND	yes	yes	PM

NA	Data not available
ND	Not detected
yes	Detected in multiple samples
yes	Detected in only one sample

[1] Ast., astrocytoma; Oligo., oligodendroglioma; GBM, glioblastoma; OA., Oligoastrocytoma.
*: No of samples successfully subtyped with both metagene projection and centroid-based SSP.
CNV results for IVY GAP and TCGA samples are based on SNP6.0 array.

Supplementary Table S5 Clinical information for SC-RNA-seq samples analyzed.

Dataset	Patient ID	Age at Diagnosis (years)	Gender	Histology	Location	WHO Grade	Copy Number Alteration	*IDH* status	MGMT promoter methylation	Numbers of Cell (passing QC)
CGGA (GSE117891)	GS1	34	F	GBM (O-included)	NA	IV	7+/10-	WT	Methylated	377
	GS2	44	M	GBM	NA	IV	7+/10-	WT	Methylated	258
	GS3	66	F	GBM	NA	IV	No Combined-CNA	WT	NM	355
	GS5	64	F	GBM	NA	IV	7+/10-	WT	NM	326
	GS6	51	M	GBM (O-included)	NA	IV	7+/10-	WT	Methylated	355
	GS7	52	M	AOA-GBM	NA	III-IV	7+/10-	WT	NM	317
	GS8	29	M	OA	NA	II	1p19q coldel	MUT	Methylated	254
	GS9	44	M	OA	NA	II	1p19q coldel	MUT	NA	364
	GS11	48	M	GBM	NA	IV	7+/10-	WT	NA	1010
	GS12	64	M	GBM	NA	IV	7+/10-	NA	NA	633
	GS13	52	M	GBM (O-included)	NA	IV	7+/10-	WT	Methylated	978
	GS14	47	F	O	NA	II	1p19q coldel	MUT	Methylated	406
GSE70630	MGH36	67	M	oligodendroglioma, 1p19q codeleted	Right frontotemporinsular	II / III	1p19q loss	MUT	NA	788
	MGH53	31	M	oligodendroglioma, 1p19q codeleted	Left frontal	II	1p19q loss	MUT	NA	861
	MGH54	35	M	oligodendroglioma, 1p19q codeleted diffuse	Right parietal	II	1p19q loss	MUT	NA	1225
	MGH60	51	M	glioma(astrocytoma), 1p19q codeleted	Left frontotemporinsular	II	1p19q loss	MUT	NA	430
	MGH93	65	F	oligodendroglioma, 1p19q codeleted	Right temporal	II	1p19q loss	MUT	NA	445
	MGH97	31	M	oligodendroglioma, 1p19q codeleted	left temporal	II	1p19q loss	MUT	NA	598
GSE89567	MGH42	47	F	IDH1 mutant anaplastic astrocytoma	left parietal	III	19q loss, 1p retained	MUT	NA	681
	MGH43	45	M	IDH1 mutant anaplastic astrocytoma, recurrent	right temporal	III	1p/19q retained	MUT	NA	553
	MGH44	32	M	IDH1 mutant anaplastic astrocytoma	right frontal	III	1p/19q retained	MUT	NA	624
	MGH45	32	F	IDH1 mutant glioblastoma, recurrent	left frontal	IV	1p/19q retained	MUT	NA	608
	MGH56	31	M	IDH1 mutant anaplastic astrocytoma	left parietal	III	1p/19q retained	MUT	NA	925
	MGH57	42	M	IDH1 mutant glioblastoma	right temporal	IV	1p/19q retained	MUT	NA	415
	MGH61	24	M	IDH1 mutant anaplastic astrocytoma	right frontal	III	19q loss, 1p retained	MUT	NA	1365
	MGH64	40	F	IDH1 mutant anaplastic astrocytoma	left frontoparietal	III	1p/19q retained	MUT	NA	795
	MGH103	26	F	IDH1 mutant anaplastic astrocytoma	left parietal	III	1p/19q retained	MUT	NA	113
	MGH107	47	F	IDH1 mutant diffuse astrocytoma	right frontal	II	1p/19q retained	MUT	NA	261
	MGH66	67	M	GBM	Left frontal	IV	7+/10-	WT	Methylated	436
	MGH100	71	F	GBM	Left frontal	IV	7+/10-	WT	Methylated	209
	MGH101	52	M	GBM	Left frontal	IV	7+/10-	WT	NM	200
	MGH102	65	M	GBM	Left temporal	IV	7+/10-	WT	NM	312
	MGH104	65	F	GBM	Right parietal	IV	7+/10-	WT	NM	355
	MGH105	67	F	GBM	Right temporal	IV	7+/10-	WT	NM	160
	MGH106	66	M	GBM	Right temporoparietal	IV	7+/10-	WT	NM	200
	MGH110	61	M	GBM	Right frontal	IV	No Combined-CNA	WT	NM	359
	MGH113	65	M	GBM	Right temporal	IV	7+/10-	WT	NM	260

GSE131928	MGH115	69	F	GBM	Right frontal	IV	No Combined-CNA	WT	NM	165
	MGH121	63	M	GBM	Left frontal	IV	7+/10-	WT	NM	297
	MGH122	63	M	GBM	Left frontal	IV	7+/10-	WT	NM	273
	MGH124	68	F	GBM	Right frontal	IV	7+/10-	WT	NM	370
	MGH125	76	M	GBM	Right frontotemporal	IV	7+/10-	WT	NM	399
	MGH128	65	F	GBM	Right temporal	IV	7+	WT	Methylated	184
	MGH129	78	M	GBM	Left temporal	IV	7+/10-	WT	NM	192
	MGH136	71	M	GBM	Right parietal	IV	7+/10-	WT	NM	231
	MGH143	62	M	GBM	Left frontal	IV	No Combined-CNA	WT	NM	274
	MGH151	65	M	GBM	Left parietal	IV	7+/10-	WT	NM	163
	MGH152	52	M	GBM	Left frontal	IV	7+	WT	Methylated	229

NA   Data not available
NM   Not Methylated

Supplementary Table S6 Signature genes of the cell populations identified in the EM and PM glioma samples from the CGGA dataset.

EM+	EM++	EM+++	EM+PM++	PM+++	Oligodendrocyte	Microglia/ Macrophage	T cells
AK1	ACSS3	ACSBG1	AFAP1L2	ACSL6	ABCA2	ADAM28	ABRACL
BBOF1	AGT	ADAMTS9	APOLD1	AKR1C3	ADAMTS4	ADAP2	ACAP1
C11orf70	AKAP12	ADCY1	ASPM	ALDOC	ADARB2	ADORA3	AHNAK
C11orf88	AP1S2	AFAP1L1	ATCAY	ARPP21	ADARB2-AS1	AIF1	APOBEC3C
C1orf141	AQP4	AK4	AURKB	ASIC1	AK5	ALOX5AP	APOBEC3G
C1orf158	ARHGAP29	AQP1	B4GALNT1	ATCAY	AMER2	APBB1IP	ARHGDIB
C1orf194	ARSJ	ARC	BEX5	ATP6V1G2	ANK3	APOC1	BCL11B
C5orf49	C10orf10	ATP1A2	BIRC5	BCAN	ANKS1B	BCL2A1	CCL5
C6orf118	C1R	BCR	C1QL1	BEST3	ANLN	C1QA	CD2
C7orf57	C1S	C6orf15	CA10	BMP2	APLP1	C1QB	CD247
C9orf116	C2orf80	CCDC167	CCNE2	BTBD17	APOD	C1QC	CD27
C9orf24	CA12	CCDC80	CDCA3	CALCRL	ASPA	C3	CD3D
CAPS	CAPN5	CCT6A	CENPE	CDHR1	BOK	C3AR1	CD3E
CASC1	CAV1	CDC42EP4	CENPF	CDR1	CA2	C5AR1	CD3G
CCDC113	CDH6	CDH4	CENPU	CHGA	CAPN3	CD14	CD48
CCDC146	CHI3L1	CDH5	CENPW	CHGB	CARNS1	CD53	CD5
CCDC153	CHL1	CDK6	CLSPN	CPE	CDK18	CD68	CD52
CCDC170	CHPF	CHCHD2	CNTN1	CRTAC1	CERCAM	CD74	CD69
CCDC39	CITED1	CHN1	COL11A1	CSMD3	CLDN11	CD83	CD7
CCDC65	CLU	CHRNA1	COL20A1	CSPG5	CLDND1	CD84	CD8A
CCDC74A	COL6A1	CHST8	COL9A1	CXXC4	CNDP1	CH25H	CD8B
CEP126	COL6A2	CISH	CRABP1	DGCR6	CNP	CLEC7A	CD96
CETN2	CPNE8	CLDN10	CRMP1	DLL3	CNTN2	CSF1R	CLEC2B
CFAP100	CRISPLD1	CMTR1	DCT	ENHO	CNTNAP4	CSF3R	CLEC2D
CFAP126	CXCL14	COL4A1	DCX	FAM110B	CRYAB	CTSS	CLIC3
CFAP161	CYR61	CPNE4	DLL3	FAM155A	CSRP1	CX3CR1	CORO1A
CFAP206	CYTOR	CPNE5	ELAVL4	FERMT1	EDIL3	CXCL8	CRIP1
CFAP221	DIRAS3	CREB3L1	ESCO2	FGF12	EFHD1	CYBB	CST7
CFAP43	DLK1	CRYM	EZH2	FXYD6	ELOVL1	DOCK2	CTSW
CFAP52	EGFR	DENND2A	FAM111B	GABBR1	ENPP2	EGR3	CXCR3
CFAP53	EIF3M	DGKG	FBXO5	GABRB3	ERMN	FCER1G	CYTIP
CFAP70	ELMOD1	DIO2	FGF12	GAD1	EVI2A	FCGBP	DENND2D
CFAP77	EPAS1	DSTYK	FGF14	GADD45G	FA2H	FCGR1A	DUSP2
CP	F3	EGFR	GNG3	GALNT13	FAM107B	FCGR2A	ETS1
DNAH12	FABP5	ELOVL2	GNG4	GDAP1L1	FGFR2	FCGR3A	FAM46C
DNALI1	FABP7	EN1	GPR17	GFRA1	FOLH1	FCGR3B	FCMR
DRC1	FAM84A	ETNK2	GRID2	GPM6A	GJB1	FGL2	FKBP11
DRC3	FLNA	FIGN	HIST1H2AM	GPR37	GPR37	FOLR2	FLT3LG
DRC7	FXYD1	FKBP5	HIST1H4C	GRIA2	GPRC5B	FPR1	GATA3
DTHD1	FXYD7	FMOD	HRASLS	GRIA4	GRM3	FYB	GIMAP7
DYDC2	GAP43	FOXO1	IGFBPL1	HAPLN1	HHATL	GPR183	GMFG
DYNLRB2	GDF15	GAS1	INSM1	HES5	HPN-AS1	GPR34	GNLY
EFCAB1	GJA1	GBAS	KCNQ1OT1	HES6	HSPA2	HAMP	GZMA
EFCAB10	GNG11	GLI2	KIF11	HEY1	KLK6	HAVCR2	GZMB
EFHC1	GPC1	GLO1	KIF15	HMP19	LGI3	HCK	GZMH
FAM179A	HOPX	GNAS	KIF2C	ID1	LHPP	HCLS1	GZMK
FAM183A	IGFBP2	GPRC5C	KLHL23	INA	LINC00844	HLA-DMA	HCST
FAM216B	IGFBP3	IGFBP5	LINC00643	JPH4	LOC100506725	HLA-DMB	ICAM3
FAM81B	IGFBP7	KCNIP1	LOC1019281(	KCNB1	MAG	HLA-DPA1	IFITM1
FAM92B	ITGA7	KCNQ2	LRRN2	KCNIP2	MAL	HLA-DPB1	IKZF3
FHAD1	JAG1	KLF9	LUZP2	KCNIP3	MAP6D1	HLA-DRA	IL16
FOLR1	KCNE4	LANCL2	MAP2	KLRC2	MAP7	HLA-DRB1	IL2RB
FOXJ1	KCNF1	LFNG	MEG3	LINC00643	MBP	HLA-DRB5	IL2RG
GABRG1	LGALS3	LGR6	MEX3A	LMF1	MOBP	IER3	IL32
HYDIN	LZTS1	LHFP	MFAP4	LOC286178	MOG	IFI30	IL7R
				LOC728715			

IFI27	METTL7B	LIFR	MKI67	LRRC4C	MYLK	IGSF6	ITGAL
IGFBP7-AS1	MOXD1	MDM4	MLLT11	LRRN1	MYRF	IL1B	KLRB1
IQCG	MT1E	MEOX2	MYBPHL	MAP2	NECAB1	IL1RN	LAT
KIF9	MT1F	MGLL	NEUROD1	MEGF11	NINJ2	ITGAX	LBH
LOC10272519	MT1L	MLC1	NFIB	MYT1	NKX6-2	ITGB2	LCK
LOC388780	MT1X	MRPS17	NKAIN4	MYT1L	OPALIN	KLF2	LIMD2
LRRC46	MT3	MT1M	NMU	NDRG2	PCSK6	LAPTM5	LIME1
LRRC6	MXRA7	MT1X	NNAT	NEU4	PEX5L	LAT2	LTB
LRRIQ1	NEK6	MT2A	NPPA	NKAIN4	PIP4K2A	LCP2	LY9
MAP3K19	NES	MYBPC1	NRXN1	NRXN1	PLEKHB1	LILRB4	NCF1B
MGST1	NNMT	MYO1B	NUF2	OLIG1	PLEKHH1	LST1	NKG7
MORN5	NPNT	NETO2	NUSAP1	PHYHIPL	PLLP	LTC4S	OXNAD1
NEK11	NRN1	NOS2	NXPH1	PID1	PLP1	LY86	PCED1B-AS1
NME5	PDLIM4	NPHP3	PAK3	PLPPR1	PLPP2	LYZ	PLAC8
NNAT	PIN4P1	NPTX1	PCDH7	PSD2	PPP1R14A	MNDA	PRF1
PALMD	PIPOX	NPTX2	PCP4	RAB3C	PTGDS	MS4A6A	PRKCH
PIFO	PITX2	P2RY1	PDGFRA	RGMB	PXK	MS4A7	PSTPIP1
PIH1D2	PLA2G5	PDZD2	PEG10	RGR	QDPR	MSR1	PTPN22
PPIL6	PLAT	PLEKHA6	PFN2	RIMS2	RAB40B	OLFML3	PTPRC
PPP1R42	PLEKHA4	PPP1R15B	PKIA	RTN1	RAPGEF5	OLR1	PTPRCAP
RARRES2	PON2	PSPH	PRC1	SCD5	RBP7	OSM	PVRIG
RIBC1	PPP1R1C	RBBP5	RAD51AP1	SCG3	RNASE1	P2RY12	PYHIN1
RIIAD1	PTN	RPH3A	RFC4	SCN3A	SEC14L5	P2RY13	RAC2
ROPN1L	PTX3	SEC14L1	RIT2	SCN3B	SEMA3B	PLAUR	RHOH
RSPH1	RCAN1	SEZ6	RND3	SERPINE2	SEPT4	PLD4	RUNX3
RSPH4A	RCN1	SLC24A3	SCG3	SEZ6L	SEPT8	PLEK	S100A4
SAMD15	RDH10	SLC4A4	SGO1	SHD	SERPINI1	PLXDC2	SAMD3
SLC47A2	RGS6	SMIM3	SNAP25	SLC1A2	SH3GL3	PTAFR	SEPT1
SPA17	RNF180	SNRPE	SNX22	SLC24A3	SH3TC2	PTGS2	SH2D1A
SPAG1	S100A16	SOCS2	SOX11	SLC25A18	SLAIN1	RGS1	SH2D2A
SPAG17	SCG2	SOX13	SOX4	SLIT1	SLC24A2	RGS10	SIT1
SPAG8	SEC61G	SPRY4	SOX6	SMIM18	SLC31A2	RGS2	SKAP1
SPATA17	SEMA3A	SRPX	SPC25	SMOC1	SLC48A1	RHBDF2	SLFN5
SPEF2	SERPINH1	SUMF2	STMN2	SNAP91	SLC5A11	RNASET2	SPOCK2
TCTEX1D1	SMS	TMEM81	TCEAL2	SNTG1	SLCO1A2	S100A8	STAT4
TEKT1	SOCS2	TRIO	TCEAL5	SOX8	SPOCK3	S100A9	STK17B
TMEM190	SPOCD1	TSPAN12	TCEAL6	SPARCL1	ST18	SAMSN1	SUPT3H
TPPP3	SRPX	UHRF1	THSD7A	SPHKAP	TF	SERPINA1	TBC1D10C
TTC25	TIMP1	VOPP1	TM4SF1	ST6GAL2	TMEM125	SLCO2B1	TC2N
VWA3A	TNC	WIPF3	TMEM132B	TNK2	TMEM144	SRGN	THEMIS
WDR38	TNFRSF12A	ZBED6	TMSB15A	TNR	TPPP	TMEM52B	TIGIT
WDR63	TUBB6	ZBTB16	TOP2A	TOX	TTYH2	TREM1	TNFAIP3
WDR78	UPP1	ZC3H11A	TP73	TUSC3	TUBB4A	TREM2	TRAF3IP3
ZBBX	VIM	ZFYVE21	UBE2C	UNC79	UGT8	TYROBP	TUBA4A
ZMYND10	ZAK	ZNF713	UBE2T	ZDHHC22	USH1C	VSIG4	ZAP70

Supplementary Table S7 Top five most significant GO terms in the signature genes of the malignant cell populations.

Cluster	Term	Count	%	PValue	List Total	Fold Enrichment	FDR
EM++	GO:0001558~regulation of cell growth	6	6	6.93E-05	91	13.84	0.0316917
	GO:0071276~cellular response to cadmium ion	4	4	9.59E-05	91	43.42	0.0316917
	GO:0071294~cellular response to zinc ion	4	4	1.36E-04	91	38.85	0.0316917
	GO:0045926~negative regulation of growth	4	4	1.36E-04	91	38.85	0.0316917
	GO:0031076~embryonic camera-type eye development	3	3	0.00151	91	50.33	0.2452084
EM+++	GO:0045926~negative regulation of growth	4	4	0.00014	92	38.43	0.1047958
	GO:0071294~cellular response to zinc ion	3	3	0.00468	92	28.82	0.9696932
	GO:0007623~circadian rhythm	4	4	0.00785	92	9.73	0.9696932
	GO:0048589~developmental growth	3	3	0.00804	92	21.90	0.9696932
	GO:0006813~potassium ion transport	4	4	0.01002	92	8.90	0.9696932
EM+PM++	GO:0007059~chromosome segregation	9	9	2.1E-09	88	25.26	1.431E-06
	GO:0007067~mitotic nuclear division	13	13	5.5E-09	88	10.00	1.833E-06
	GO:0007062~sister chromatid cohesion	9	9	6E-08	88	16.67	1.325E-05
	GO:0051301~cell division	13	13	2.4E-07	88	7.09	4.051E-05
	GO:0051983~regulation of chromosome segregation	3	3	0.00073	88	71.56	0.0971296
PM+++	GO:0007268~chemical synaptic transmission	8	8	0.00027	89	6.29	0.1675407
	GO:0007399~nervous system development	8	8	0.00077	89	5.26	0.1734463
	GO:0034220~ion transmembrane transport	7	7	0.00082	89	6.29	0.1734463
	GO:0007165~signal transduction	15	15	0.00275	89	2.44	0.3669742
	GO:0030154~cell differentiation	9	9	0.0029	89	3.68	0.3669742