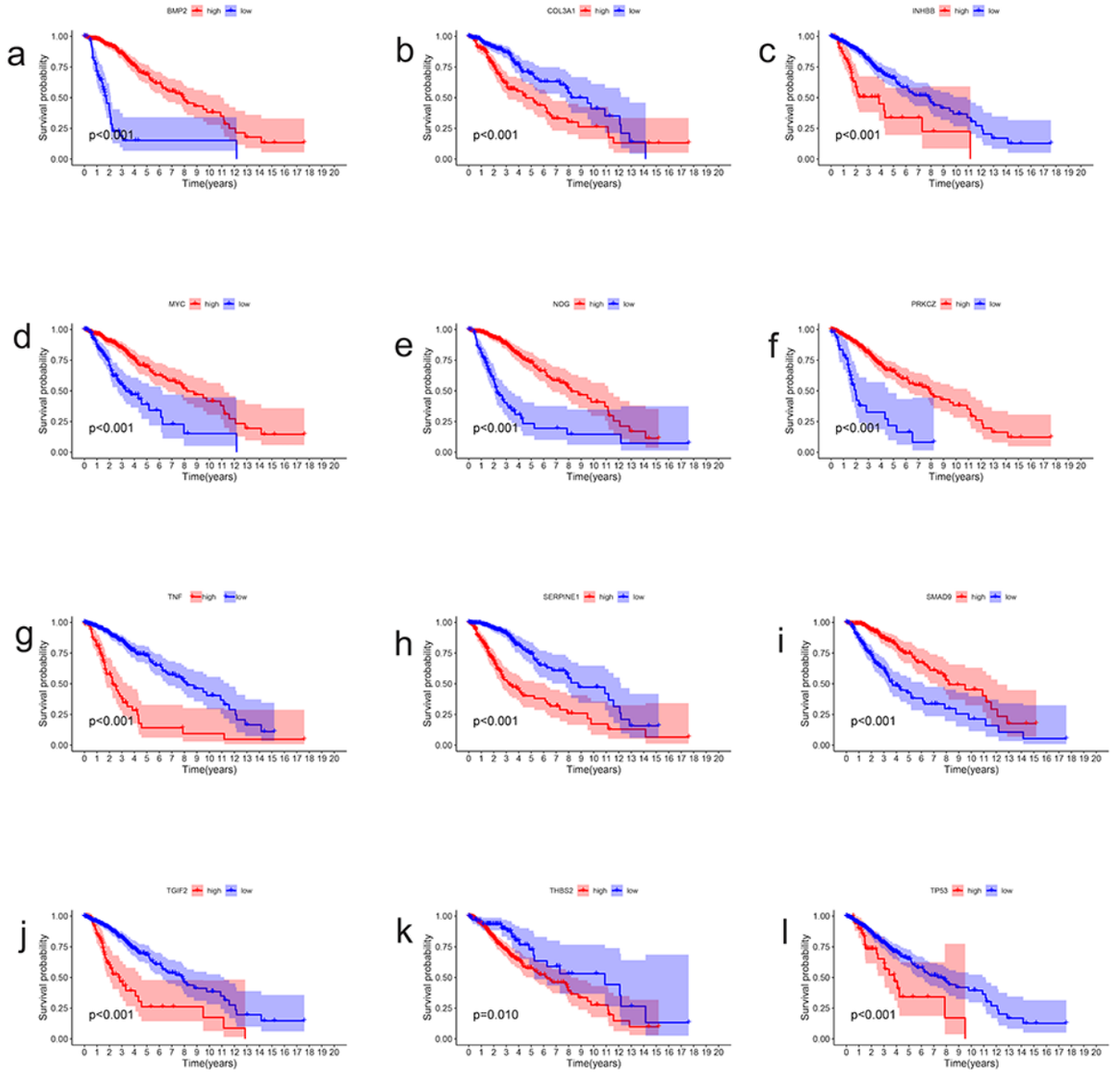

Figure S1 Survival analysis of the 12 differential and prognostic TGF-β-related genes (A-L) in TCGA dataset. TGF-β, transforming growth factor-beta; TCGA, The Cancer Genome Atlas.

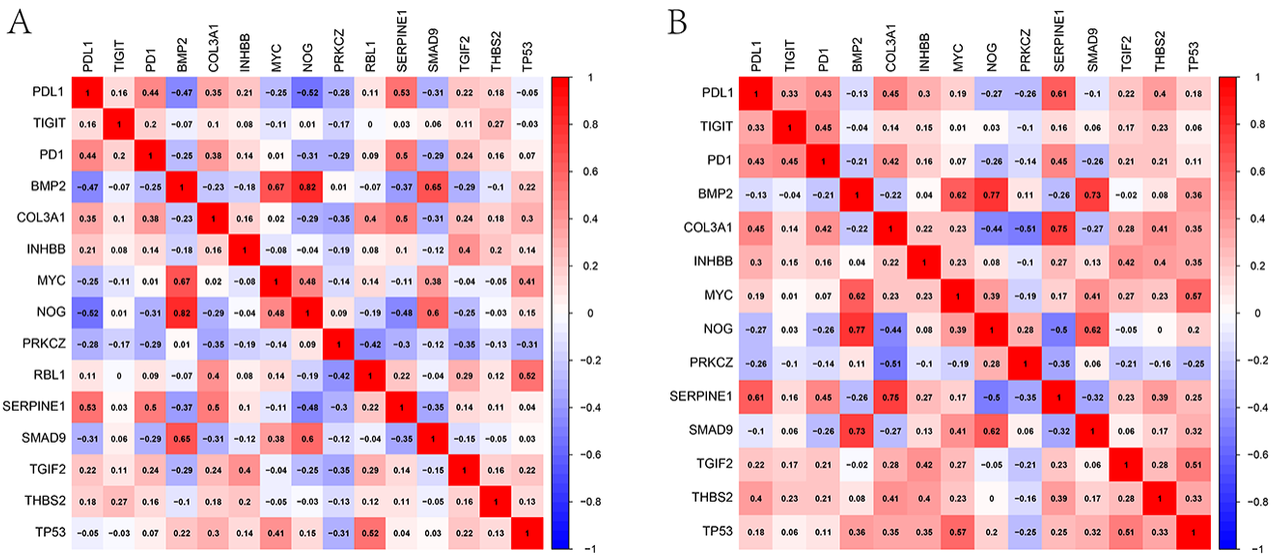

Figure S2 The correlation between TGF-β-related genes and ICPs. (A) TCGA dataset; (B) CGGA dataset. TGF-β, transforming growth factor-beta; TCGA, The Cancer Genome Atlas; CGGA, Chinese Glioma Genome Atlas.

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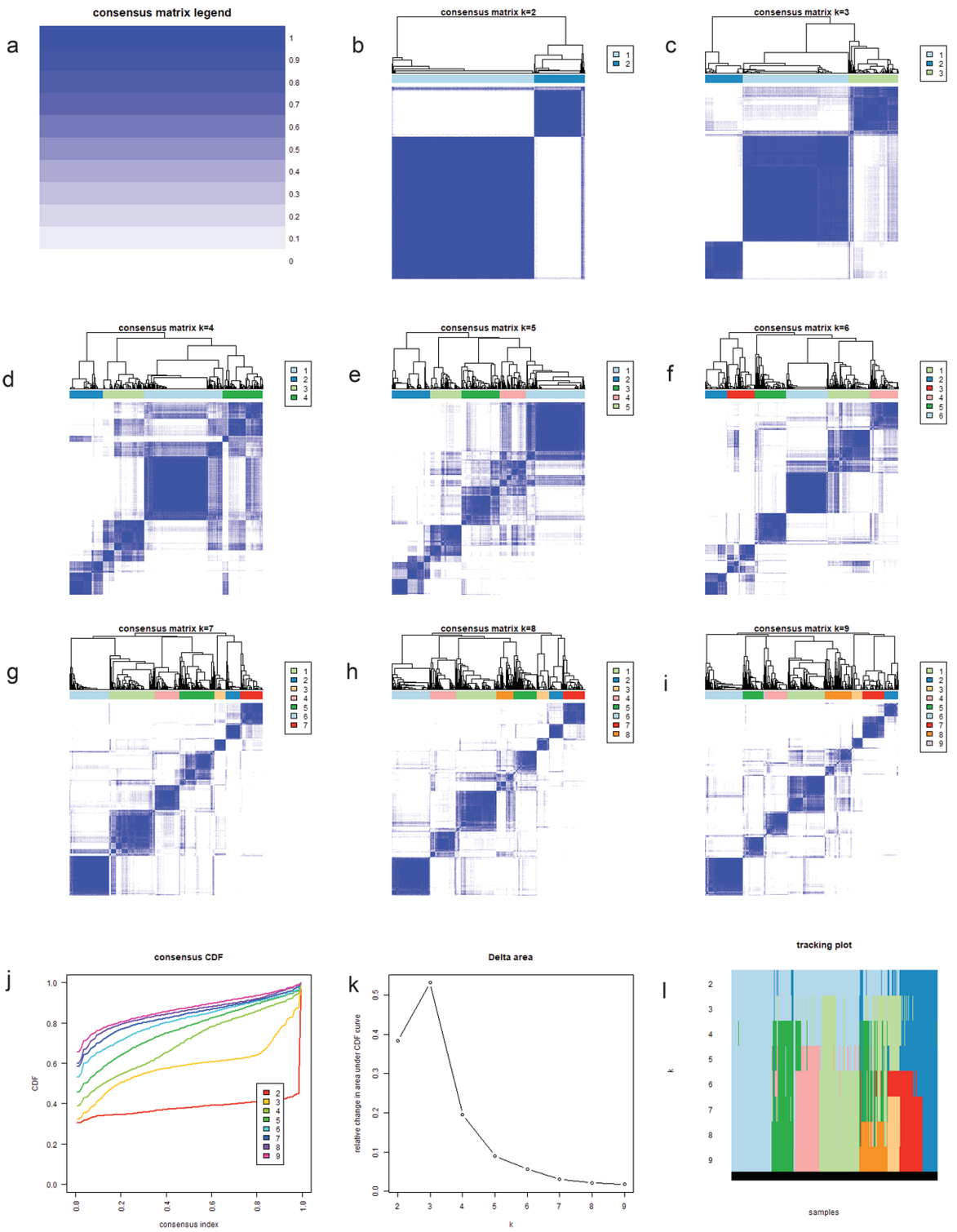

Figure S3 Consensus clustering based in metabolism gene expression of TCGA diffuse LGGs. (A-I) Clustering matrix for k=2 to k=9, Cumulative distribution function curve for k=2 to k=9; (J-L) relative change in area under the cumulative distribution function curve for k=2 to k=10. CDF, cumulative distribution function; TCGA, The Cancer Genome Atlas; LGG, low-grade glioma.

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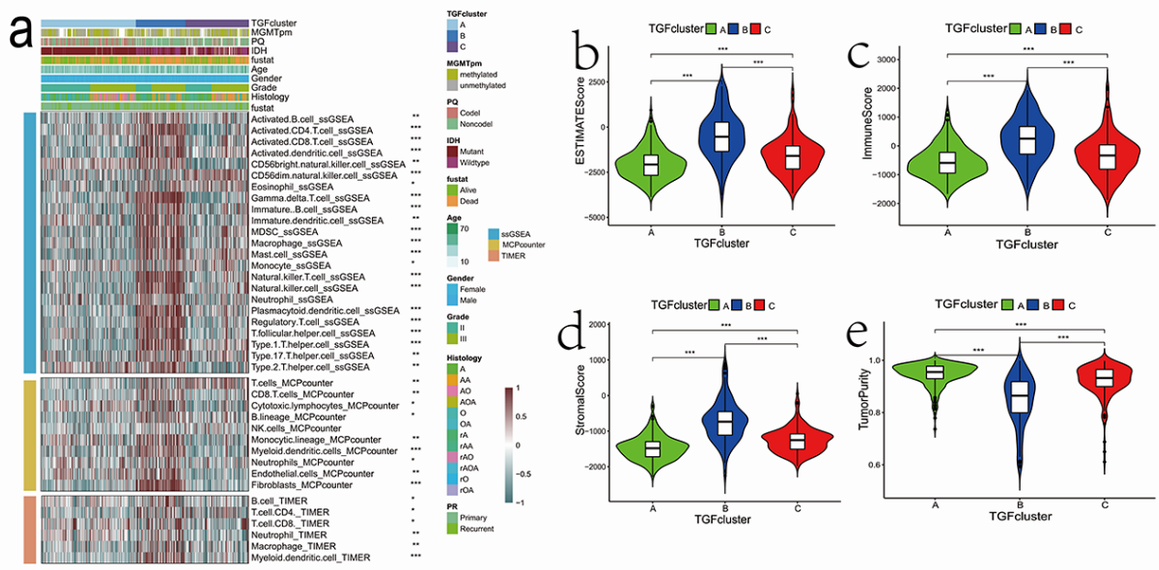

Figure S4 Infiltration of immune cells associated with TGF-β subtypes in CGGA dataset (A); ESTIMATE, immune, stromal scores and tumor purity in TGF-β subtypes (B-E). *, P<0.05; **, P<0.01; ***, P<0.001. TGF, transforming growth factor; PQ, 1p19q; *IDH*, isocitrate dehydrogenase; ssGSEA, single-sample GSEA; GSEA, Gene Set Enrichment Analysis; A, astrocytoma; AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; AOA, anaplastic oligodendrocyte astrocytoma; O, oligodendroglioma; OA, oligodendrocyte astrocytoma; r, recurrent; PRS, primary recurrence and secondary; CGGA, Chinese Glioma Genome Atlas; ESTIMATE, Estimation of STromal and Immune cells in MAlignant Tumor tissues using Expression data.

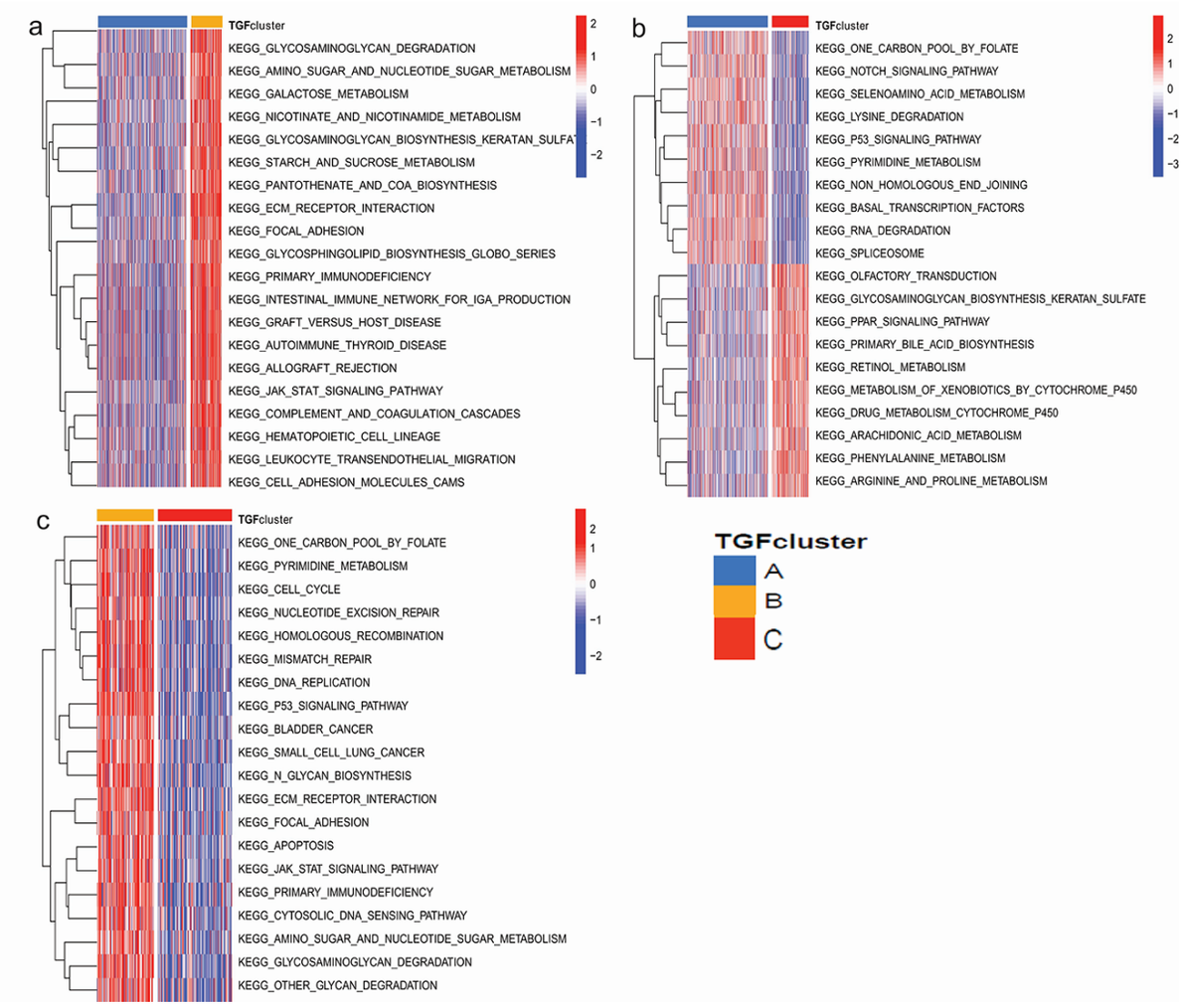

Figure S5 The top 20 potential biological functions between TGF-β subtypes in TCGA (A-C). TGF, transforming growth factor; KEGG, Kyoto Encyclopedia of Genes and Genomes; TCGA, The Cancer Genome Atlas.

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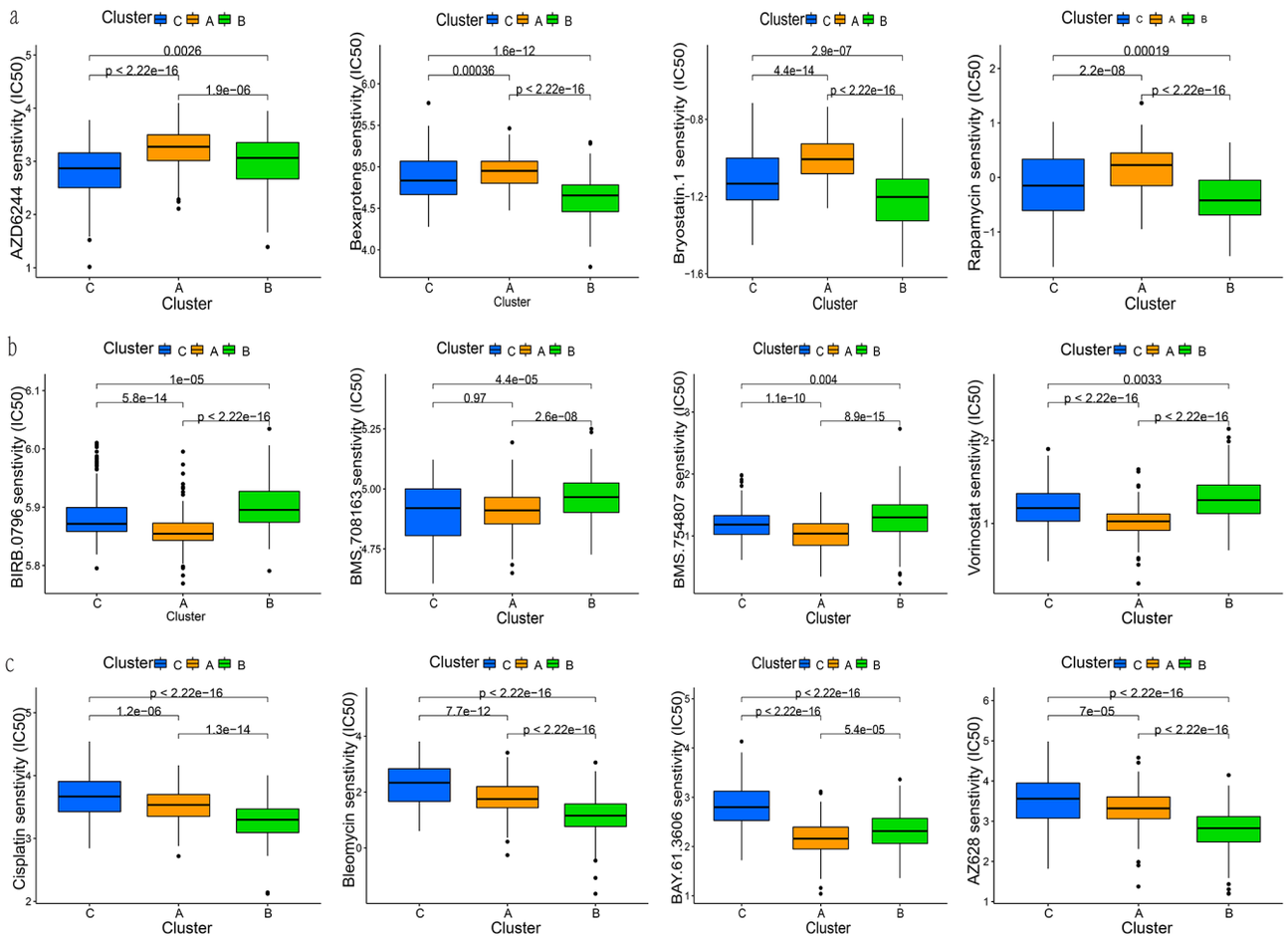

Figure S6 Drug sensitivity associated with TGF-β subtypes. (A) AZD6244, bexarotene, bryostatin 1, and rapamycin illustrated a high sensitivity for subtype A; (B) the highest drug sensitivity of BIRB.0796, BMS.708163, BMS.754807, and vorinostat was identified in subtype B; (C) cisplatin, bleomycin, BAY.61.3606, and AZ628 showed the highest sensitivity in subtype C. IC_{50}, half-maximal inhibitory concentration; TGF-β, transforming growth factor-beta.

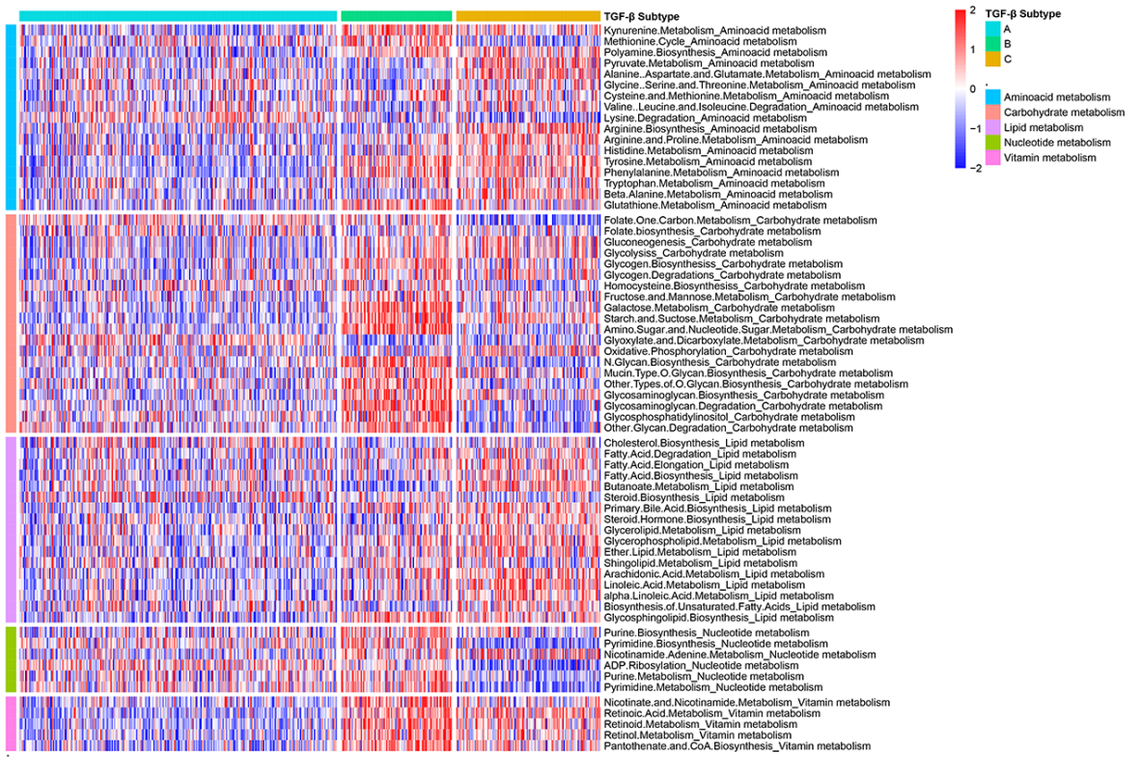

Figure S7 The metabolic characteristics of each TGF-β subtype in the TCGA database. TGF-β, transforming growth factor-beta; TCGA, The Cancer Genome Atlas.

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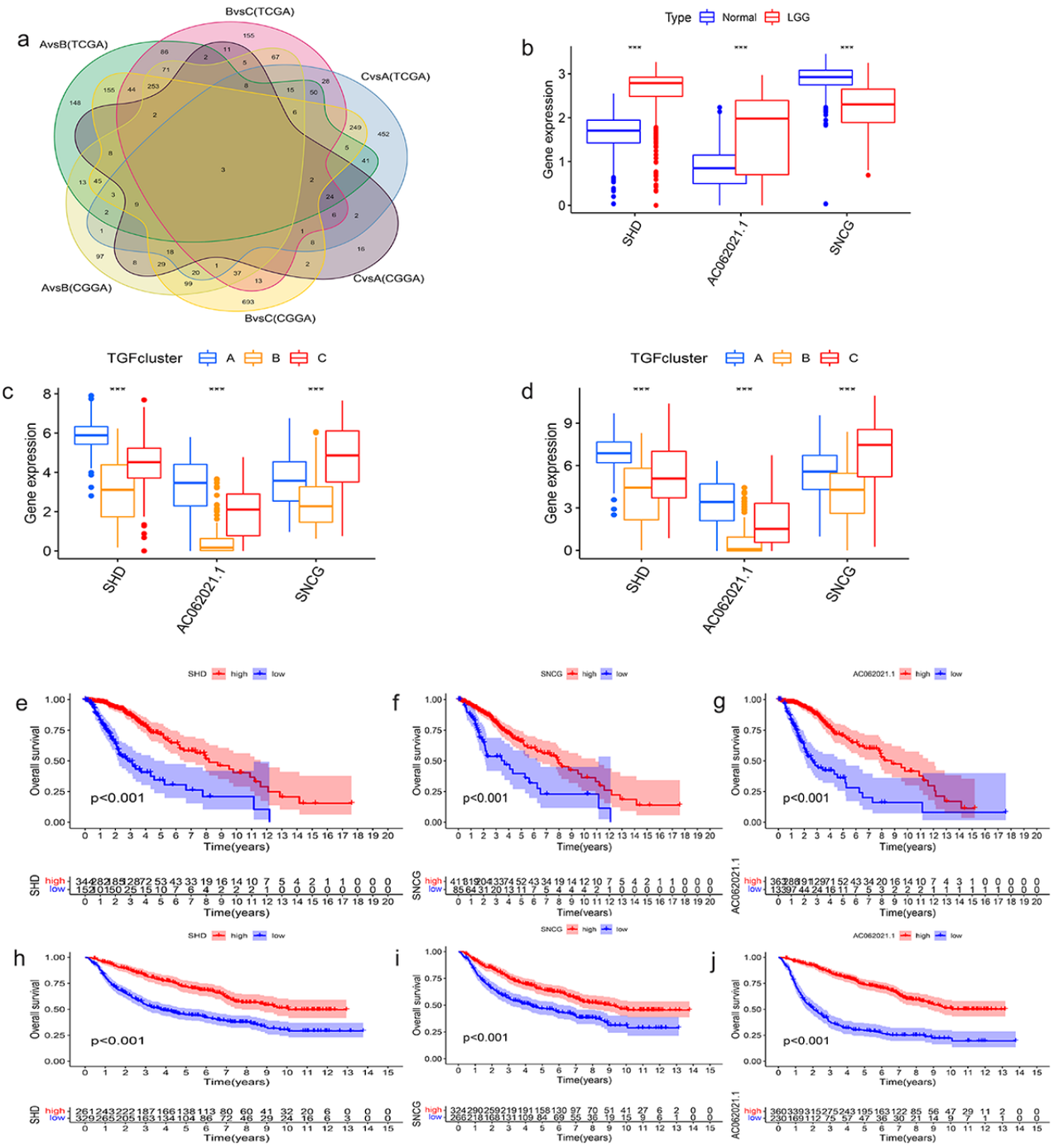

Figure S8 Identification of the differentially expressed and prognostic genes among TGF-β subtypes. (A) Venn diagram showing the three genes obtained from TGF-β subtype of TCGA and CGGA cohorts; (B) the expression of the three genes between LGG and brain normal tissues; (C) the expression of the three genes in TGF cluster; (D) the expression of the three genes in subtypes based on *IDH* mutation and 1p19q co-deletion; (E-G) survival graph describing the survival of *SHD*, *SNCG*, and *AC062021.1* in patients with LGG of TCGA cohort; (H-J) survival graph describing the survival of *SHD*, *SNCG*, and *AC062021.1* in patients with LGG of CGGA cohort. ***, P<0.001. TCGA, The Cancer Genome Atlas; CGGA, Chinese Glioma Genome Atlas; LGG, low-grade glioma; TGF, transforming growth factor; *IDH*, isocitrate dehydrogenase.

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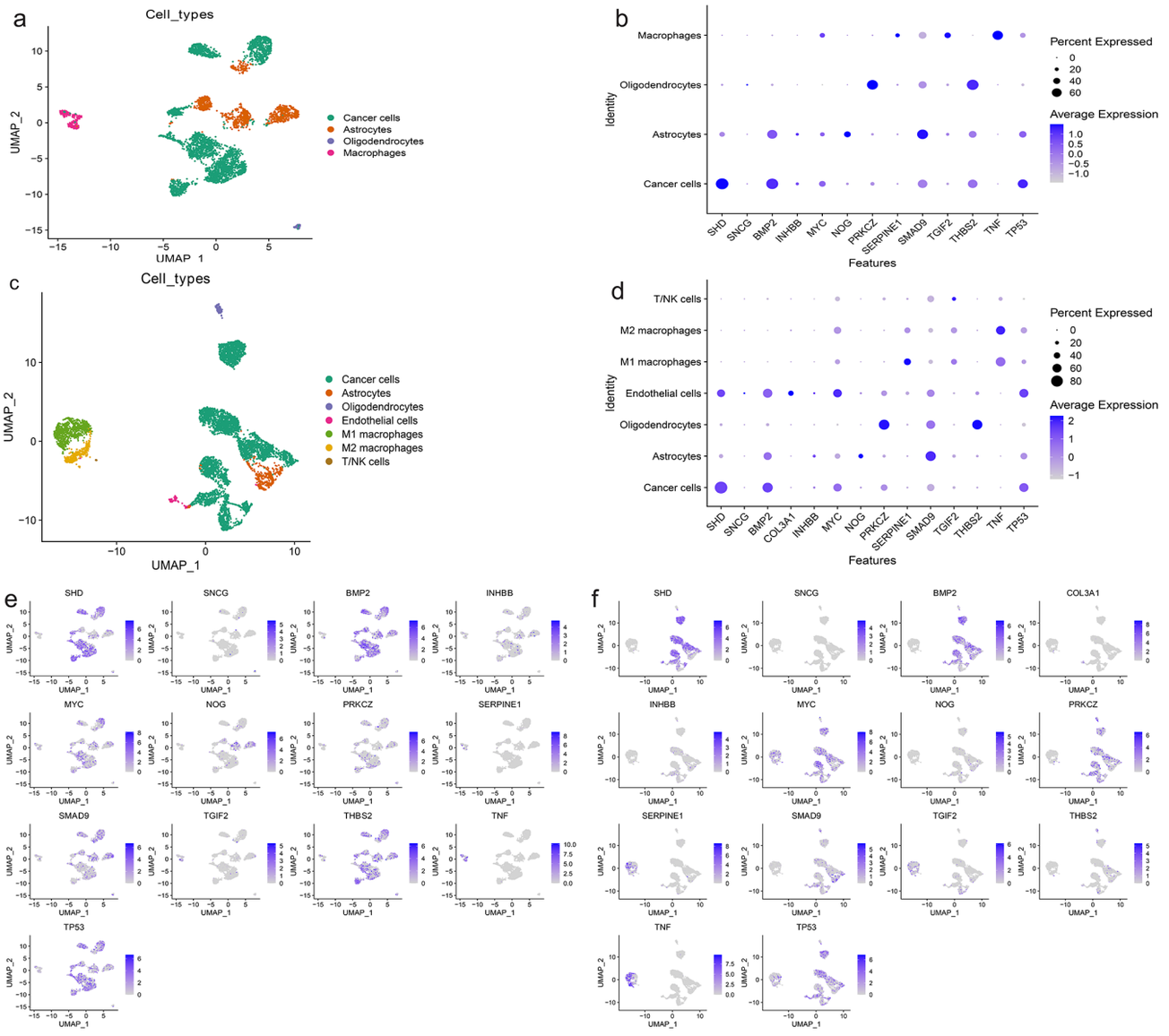

Figure S9 Single-cell RNA analysis of differentially expressed and prognostic genes in tumor or stromal cells. (A) UMAP displays the cellular populations defined by marker genes in GSE70630 dataset; (B) DotPlots show the expression levels of differential and prognostic TGF-β-related genes and *SHD*, *SNCG* in macrophages, oligodendrocytes, astrocytes, and tumor cells in GSE70630 dataset; (C) UMAP displays the cellular populations defined by marker genes in GSE89567 dataset; (D) DotPlots show the expression levels of differential and prognostic TGF-β-related genes and *SHD*, *SNCG* in macrophages, oligodendrocytes, astrocytes, T/NK cells, endothelial cells, and tumor cells in GSE89567 dataset; (E) the expression levels of differential and prognostic TGF-β-related genes and *SHD*, *SNCG* in GSE70630 dataset; (F) the expression levels of differential and prognostic TGF-β-related genes and *SHD*, *SNCG* in GSE89567 dataset. UMAP, Uniform Manifold Approximation and Projection; TGF-β, transforming growth factor-beta; NK, natural killer.

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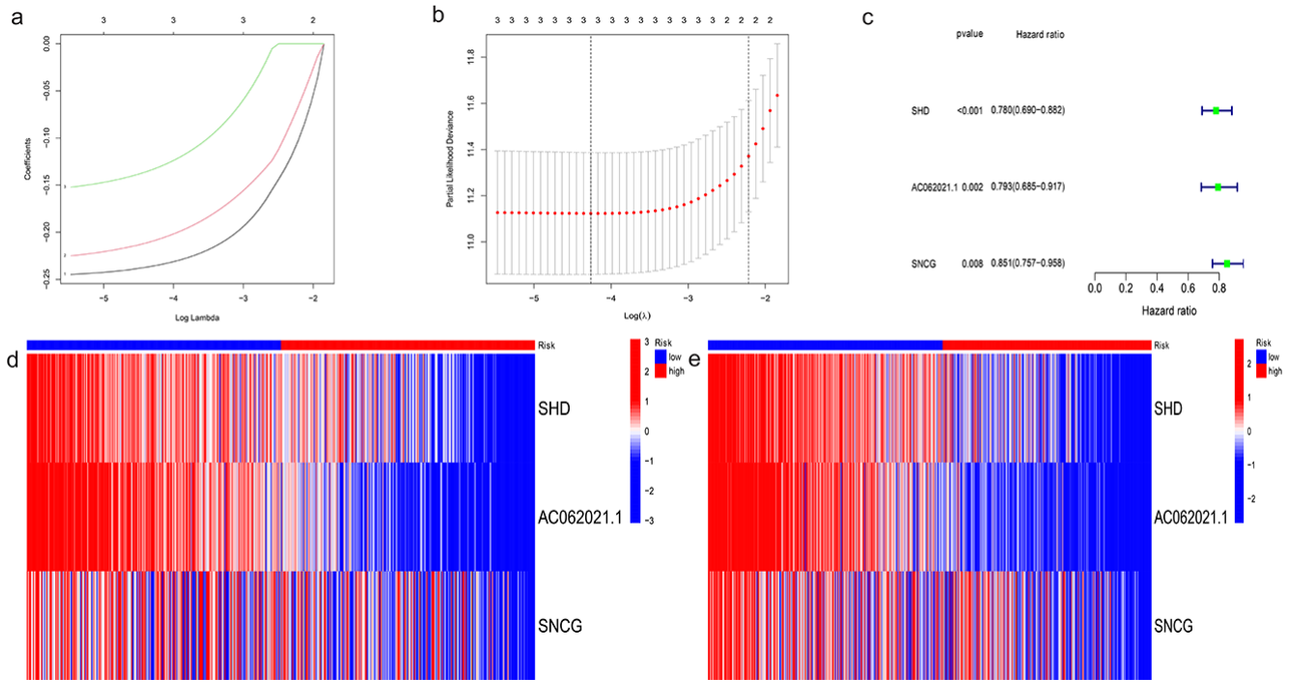

Figure S10 Calculation of a risk score based on *SHA*, *SNCG*, and *AC062021.1*. (A) Coefficient values of each signature gene; (B) partial likelihood deviance of each signature gene; (C) prognosis of *SNCG*, *SHD*, and *AC062021.1* in LGG patients by univariate analysis; (D) heatmap showing the expression levels of three signature genes in TCGA database; (E) heatmap showing the expression levels of three signature genes in CGGA dataset. LGG, low-grade glioma; TCGA, The Cancer Genome Atlas; CGGA, Chinese Glioma Genome Atlas.

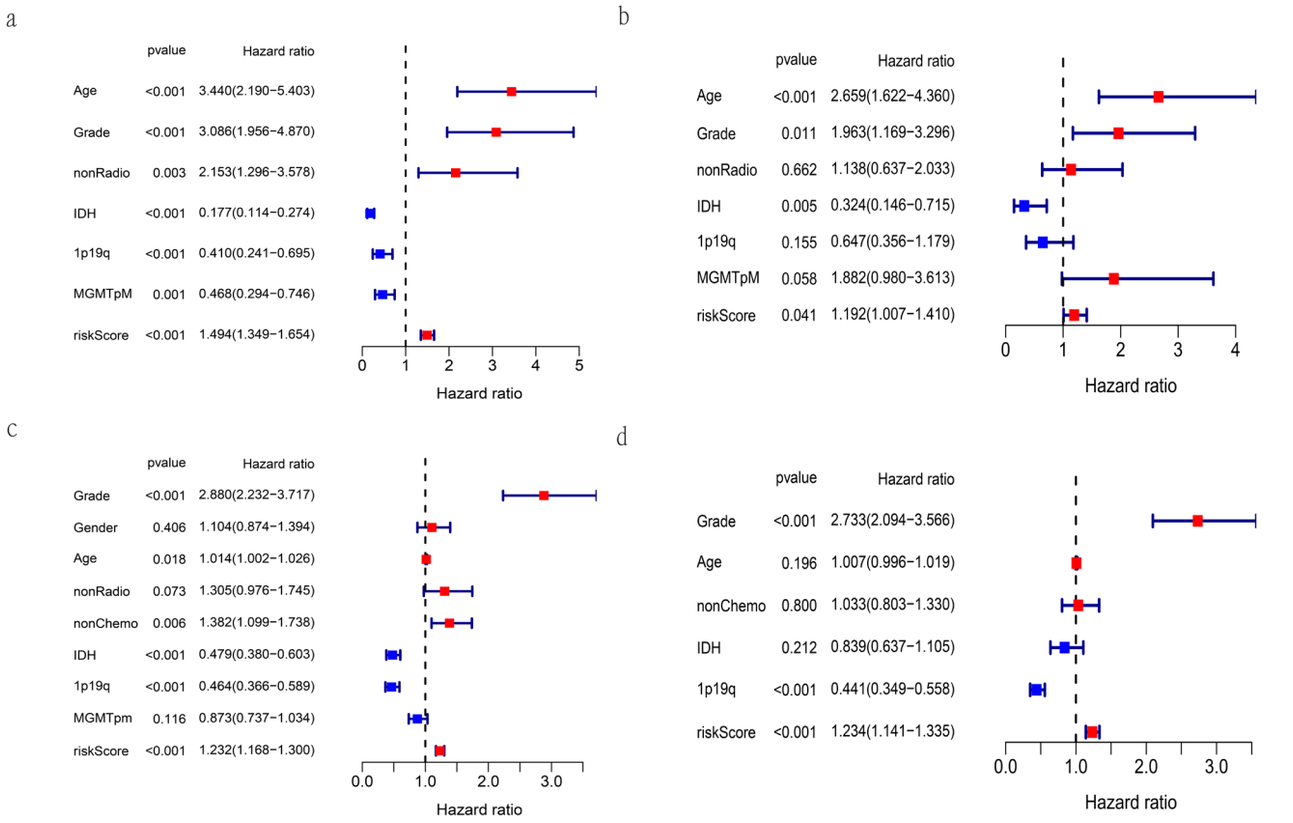

Figure S11 Univariate and multivariate Cox regression analysis of risk score in TCGA cohort (A,B) and CGGA cohort (C,D). *IDH*, isocitrate dehydrogenase; TCGA, The Cancer Genome Atlas; CGGA, Chinese Glioma Genome Atlas.

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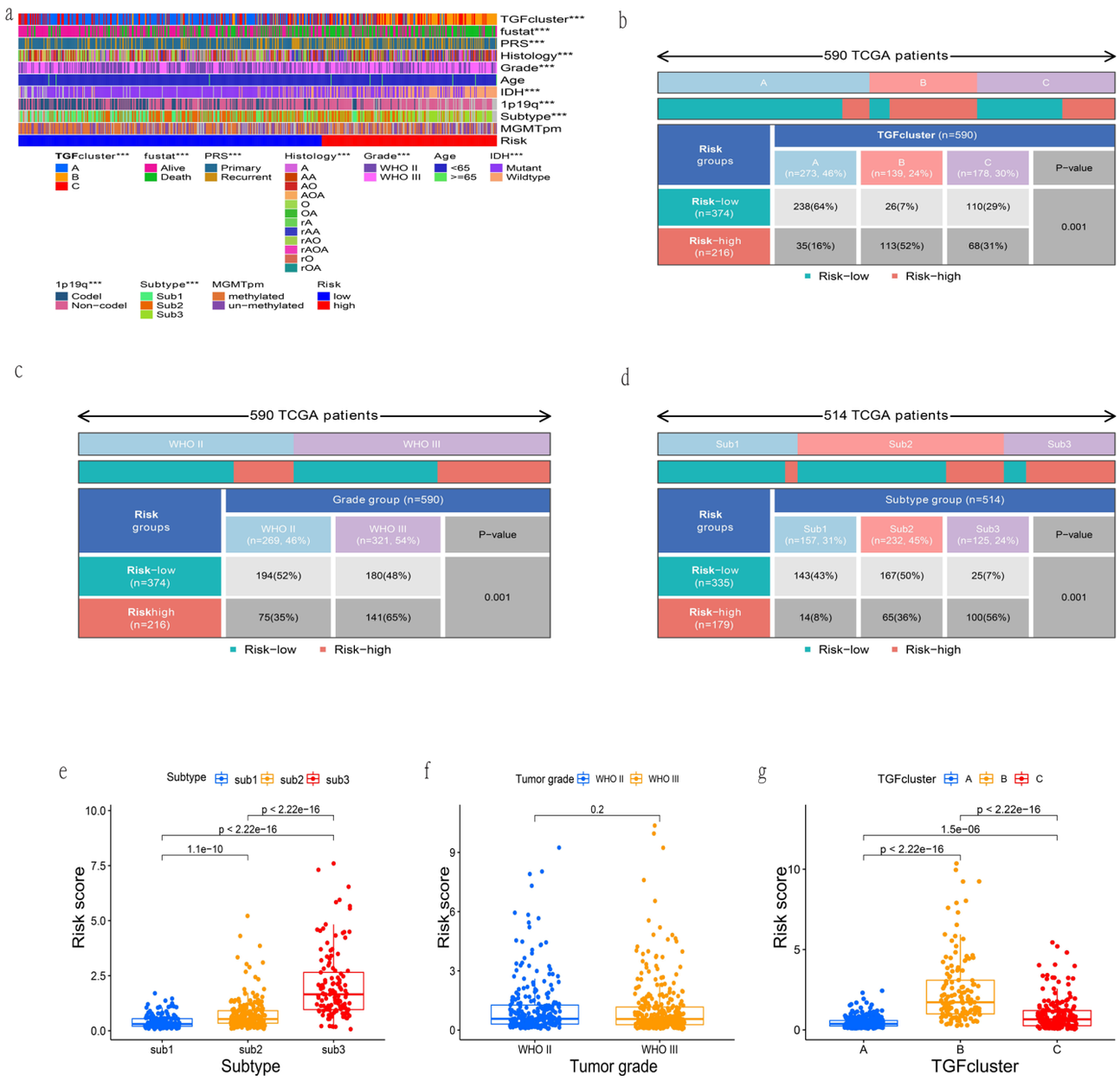

Figure S12 The characteristics of risk model in CGGA dataset. (A) Heatmap shows the clinical features between low- and high-risk group in TCGA dataset; (B-D) the relationship of TGF cluster, tumor grade, and subtype associated with risk group; (E-G) the distribution of risk score within TGF cluster, tumor grade, and subtype, respectively. ***, P<0.001. Sub1, subtype 1 (*IDH1* mutation and 1p19q codeletion); Sub2, subtype 2 (*IDH1* mutation and 1p19q no codeletion); Sub3, subtype3 (*IDH1* wild type). TGF, transforming growth factor; PRS, primary recurrence and secondary; A, astrocytoma; AA, anaplastic astrocytoma; AO, anaplastic oligodendroglioma; AOA, anaplastic oligodendrocyte astrocytoma; O, oligodendroglioma; OA, oligodendrocyte astrocytoma; r, recurrent; WHO, World Health Organization; *IDH*, isocitrate dehydrogenase; TCGA, The Cancer Genome Atlas; CGGA, Chinese Glioma Genome Atlas.

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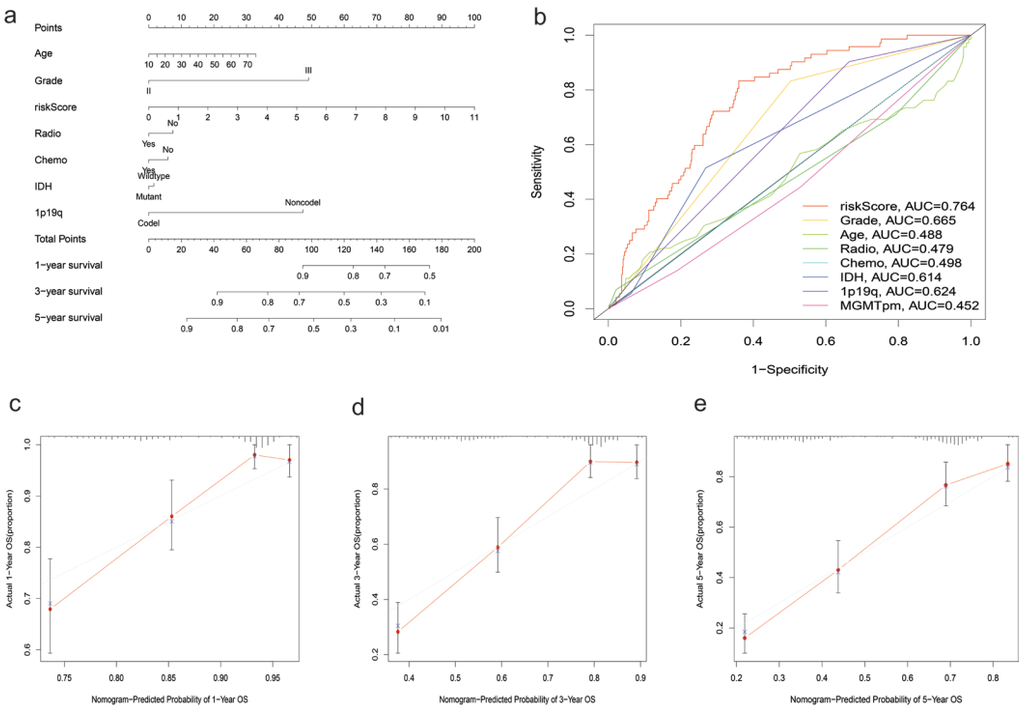

Figure S13 Prognostic nomogram based on the risk model in the CGGA cohort. (A) The nomogram based on the risk model; (B) the ROC reveals that the risk model has a higher AUC than the factors of age, *IDH* mutation status, 1p19q codeletion status, and tumor grade; (C-E) the calibration curve of 1-, 3-, and 5-year OS based on the nomogram, respectively. *IDH*, isocitrate dehydrogenase; AUC, area under the curve; OS, overall survival; CGGA, Chinese Glioma Genome Atlas; ROC, receiver operating characteristic.

Table S1 The clinical relevance TGF-β subtypes in TCGA dataset

Parameters	TGF-β cluster (n=429)			P
	A	B	C	
Age (years)				<0.0001
<45	153 (35.7)	26 (6.1)	68 (15.9)	
≥45	82 (19.1)	58 (13.5)	42 (9.8)	
Tumor grade				<0.0001
II	118 (27.5)	12 (2.8)	72 (16.8)	
III	117 (27.3)	72 (16.8)	38 (8.9)	
IDH				<0.0001
Mutant	235 (54.8)	28 (6.5)	102 (23.8)	
Wild type	0 (0.0)	56 (13.1)	8 (1.9)	
1p19q				<0.0001
Co-deletion	116 (27.0)	6 (1.4)	21 (4.9)	
Non-codeletion	119 (27.7)	78 (18.2)	89 (20.7)	
Subtype				<0.0001
Sub1	116 (27.0)	6 (1.4)	21 (4.9)	
Sub2	119 (27.7)	22 (5.1)	81 (18.9)	
Sub3	0 (0.0)	56 (13.1)	8 (1.9)	
Chemo				0.002
Yes	124 (28.9)	57 (13.3)	57 (12.8)	
No	96 (22.4)	16 (3.7)	45 (10.5)	
Na	15 (3.5)	11 (2.6)	10 (2.3)	
Radio				0.021
Yes	143 (33.3)	57 (13.3)	56 (13.1)	
No	76 (17.7)	17 (4.0)	46 (10.7)	
Na	16 (3.7)	10 (2.3)	6 (1.4)	

Data are presented as n (%). Sub1, subtype 1 (*IDH1* mutation and 1p19q codeletion); Sub2, subtype 2 (*IDH1* mutation and 1p19q no codeletion); Sub3, subtype3 (*IDH1* wild type). TGF-β, transforming growth factor-beta; TCGA, The Cancer Genome Atlas; *IDH*, isocitrate dehydrogenase; Na, not available.

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Table S2 The clinical relevance TGF-β subtypes in CGGA dataset

Parameters	TGF-β cluster (n=590)			P
	A	B	C	
Age (years)				0.024
<45	196 (33.2)	95 (16.1)	106 (18.0)	
≥45	77 (13.1)	44 (7.5)	72 (12.2)	
Tumor grade				<0.0001
II	148 (25.1)	42 (7.1)	79 (13.4)	
III	125 (21.2)	97 (16.4)	99 (16.8)	
IDH				<0.0001
Mutant	264 (44.7)	64 (10.8)	86 (14.6)	
Wild type	5 (0.8)	75 (12.7)	58 (9.8)	
Na	4 (0.7)	0 (0.0)	34 (5.8)	
1p19q				<0.0001
Co-deletion	135 (22.9)	10 (1.7)	35 (5.9)	
Non-codeletion	131 (22.2)	120 (20.3)	121 (20.5)	
NA	7 (1.2)	9 (1.5)	22 (3.7)	
Subtype				<0.0001
Sub1	132 (22.4)	9 (1.5)	16 (2.7)	
Sub2	125 (21.2)	54 (9.2)	53 (9.0)	
Sub3	5 (0.8)	75 (12.7)	58 (9.8)	
Na	11 (1.9)	1 (0.2)	51 (8.6)	
Chemo				0.124
Yes	167 (28.3)	97 (16.4)	104 (17.6)	
No	99 (16.8)	40 (6.8)	65 (11.0)	
Na	7 (1.2)	2 (0.3)	9 (1.5)	
Radio				0.061
Yes	219 (37.1)	98 (16.6)	129 (21.9)	
No	51 (8.6)	36 (6.1)	41 (6.9)	
Na	3 (0.5)	5 (0.8)	8 (1.4)	
MGMTpM				0.099
Yes	140 (23.7)	58 (9.8)	85 (14.4)	
No	79 (13.4)	53 (9.0)	28 (4.7)	
Na	54 (9.2)	28 (4.7)	25 (4.2)	

Data are presented as n (%). Sub1, subtype 1 (*IDH1* mutation and 1p19q codeletion); Sub2, subtype 2 (*IDH1* mutation and 1p19q no codeletion); Sub3, subtype3 (*IDH1* wild type). TGF-β, transforming growth factor-beta; CGGA, Chinese Glioma Genome Atlas; *IDH*, isocitrate dehydrogenase; Na, not available.

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