

Figure S1

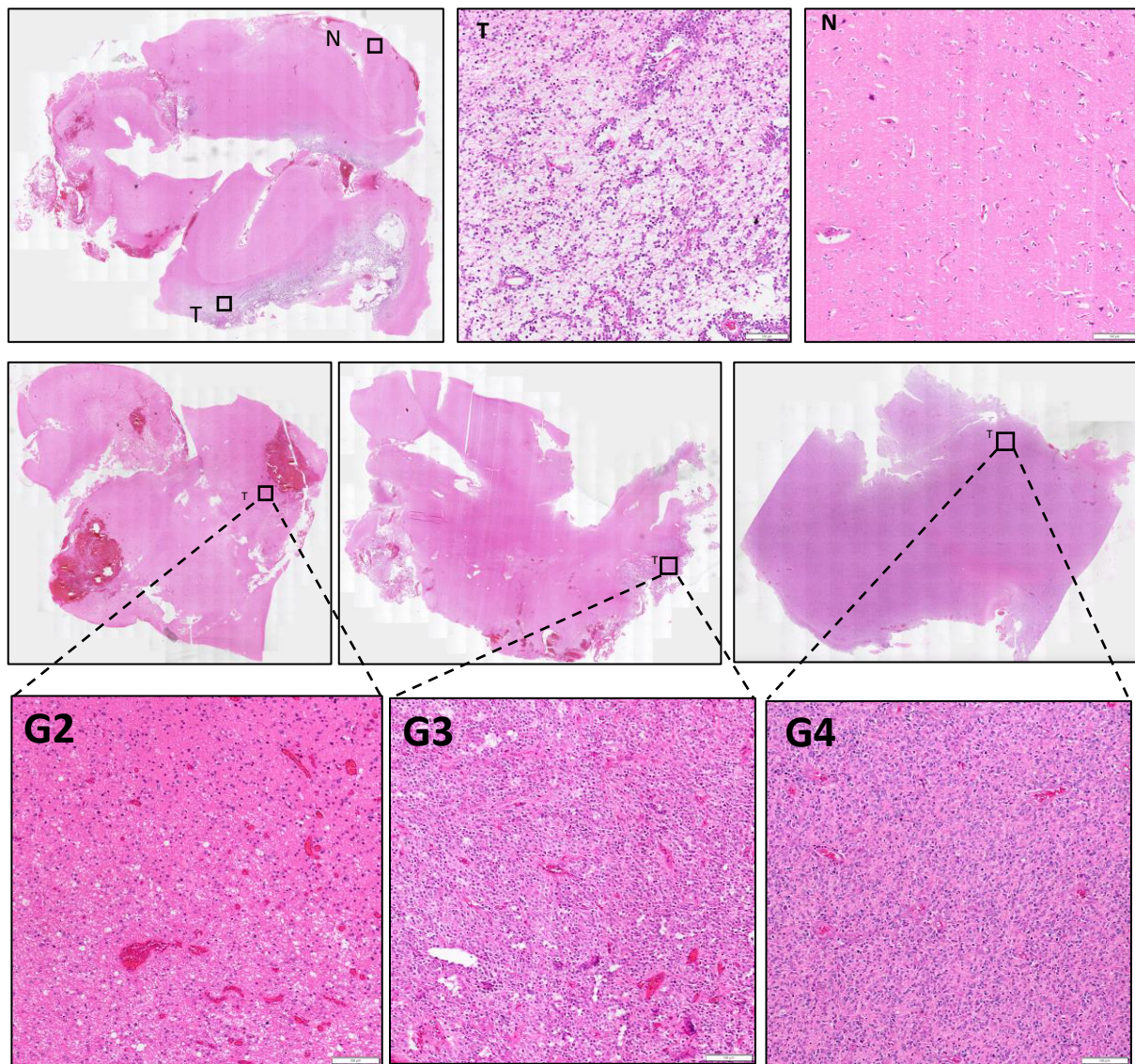


Figure S2

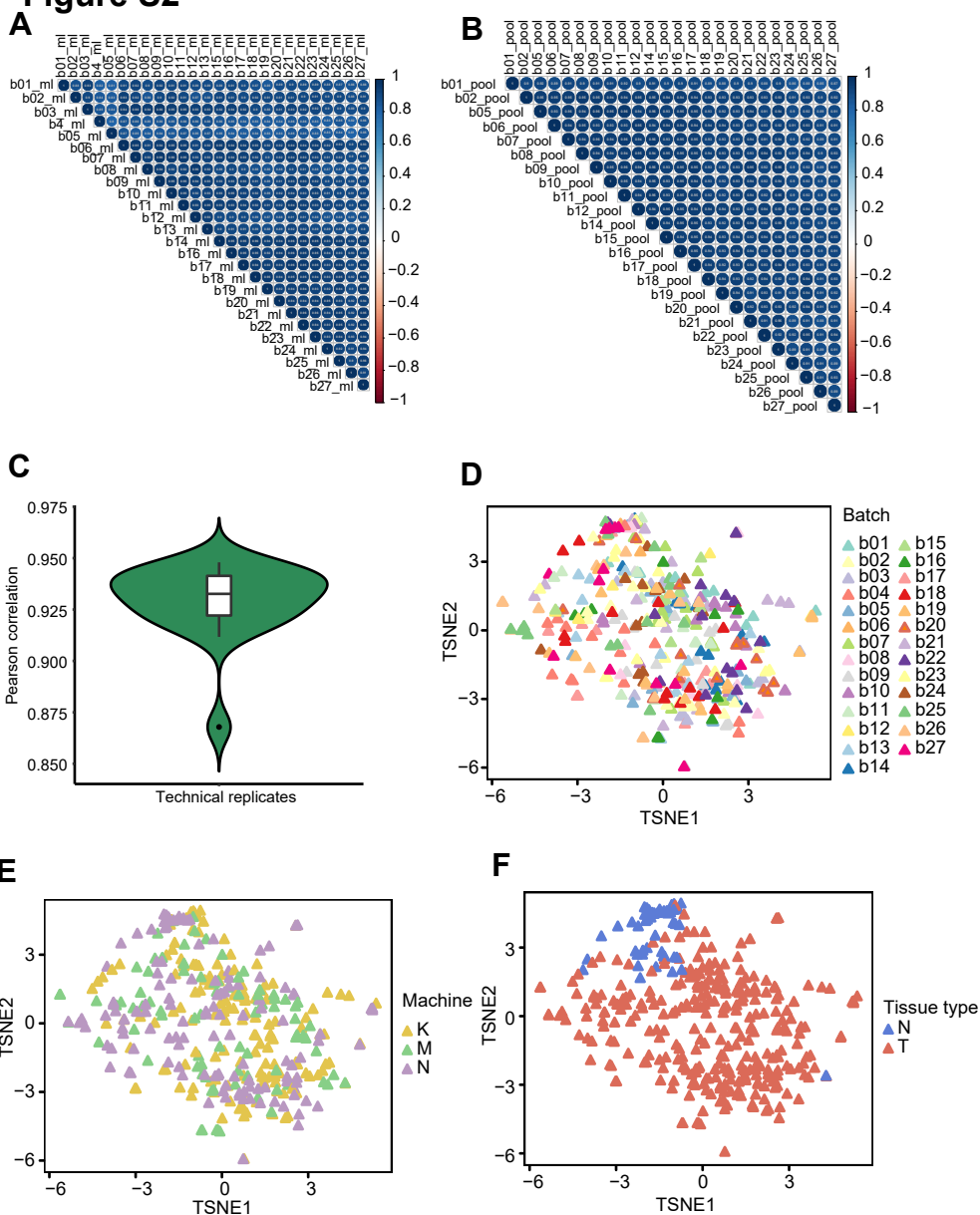


Figure S3

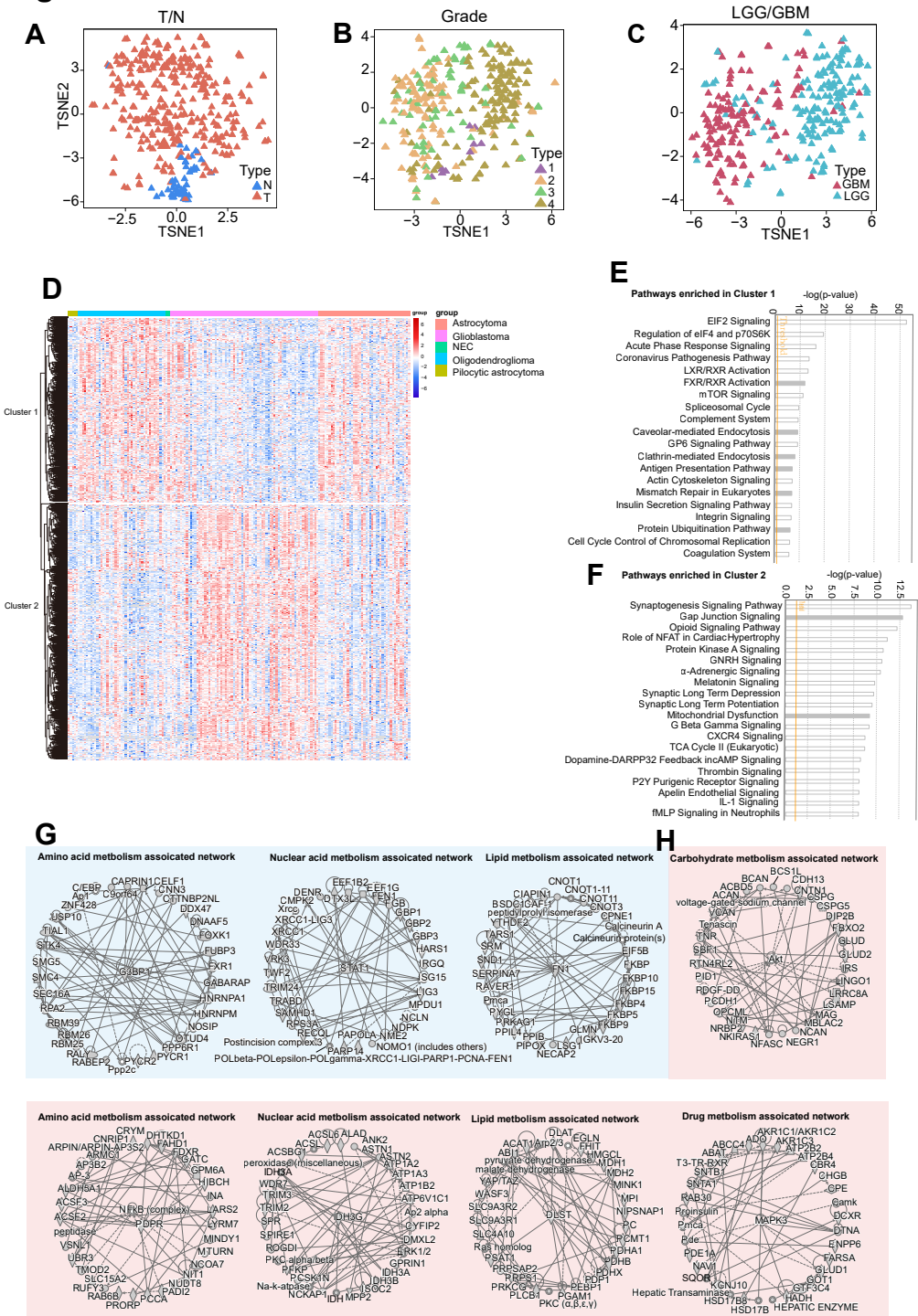


Figure S4

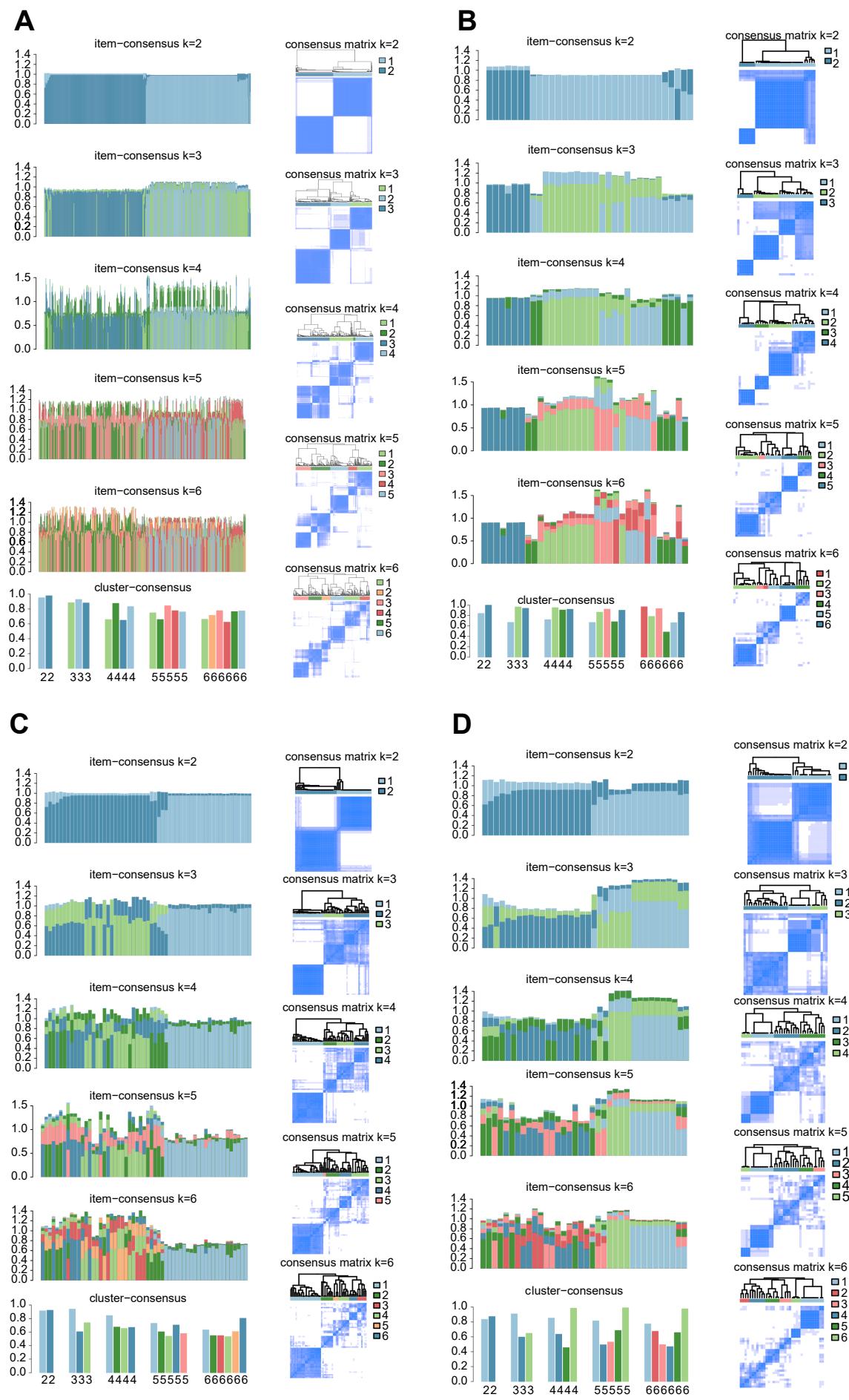


Figure S5

A

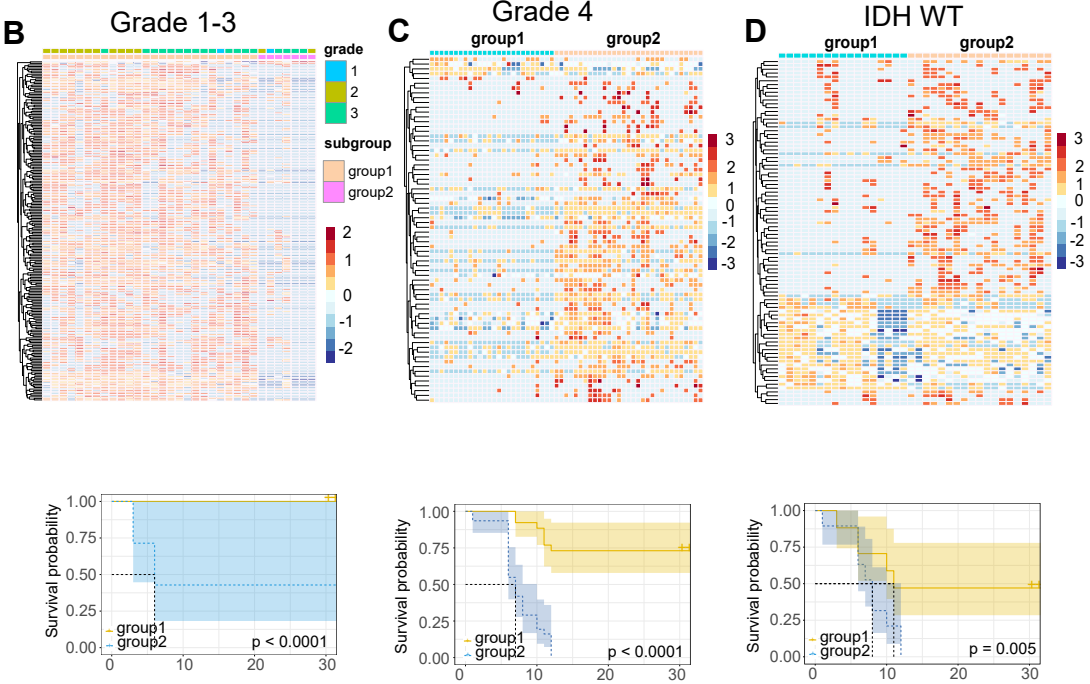
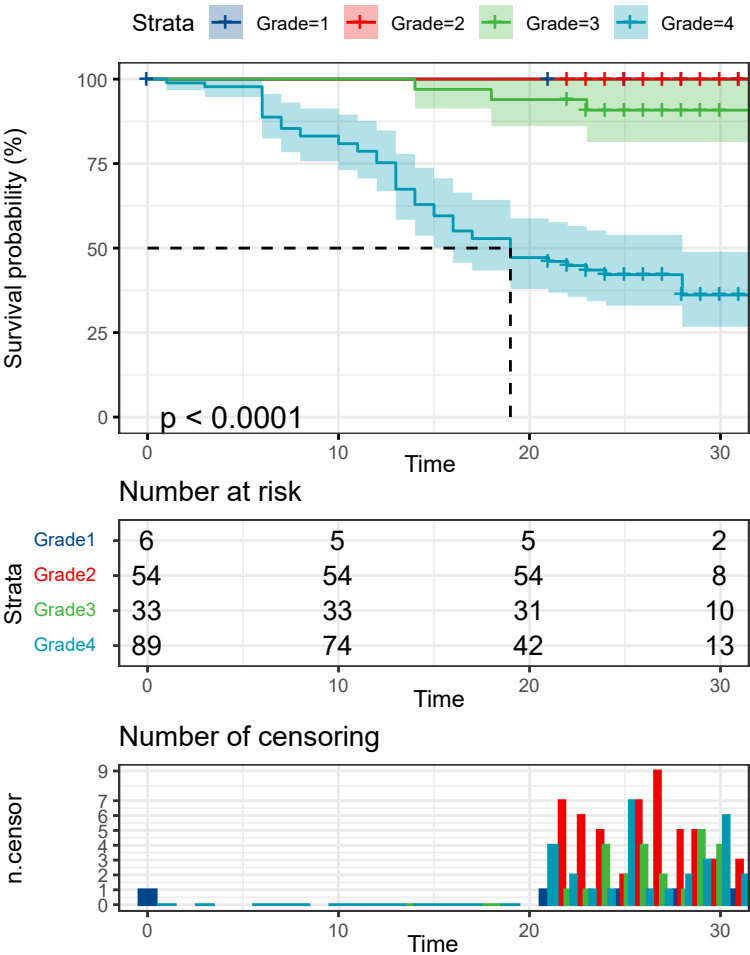


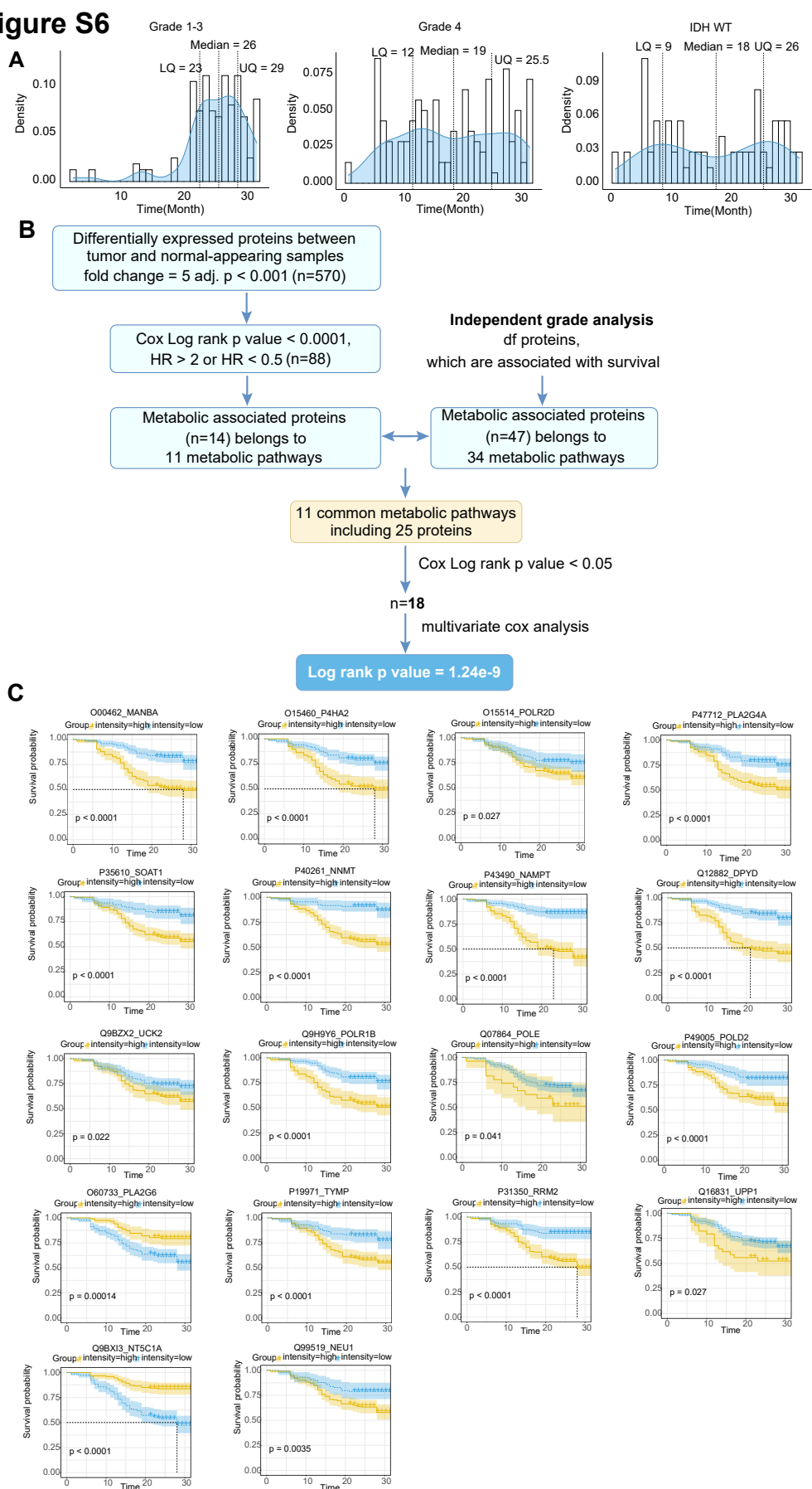
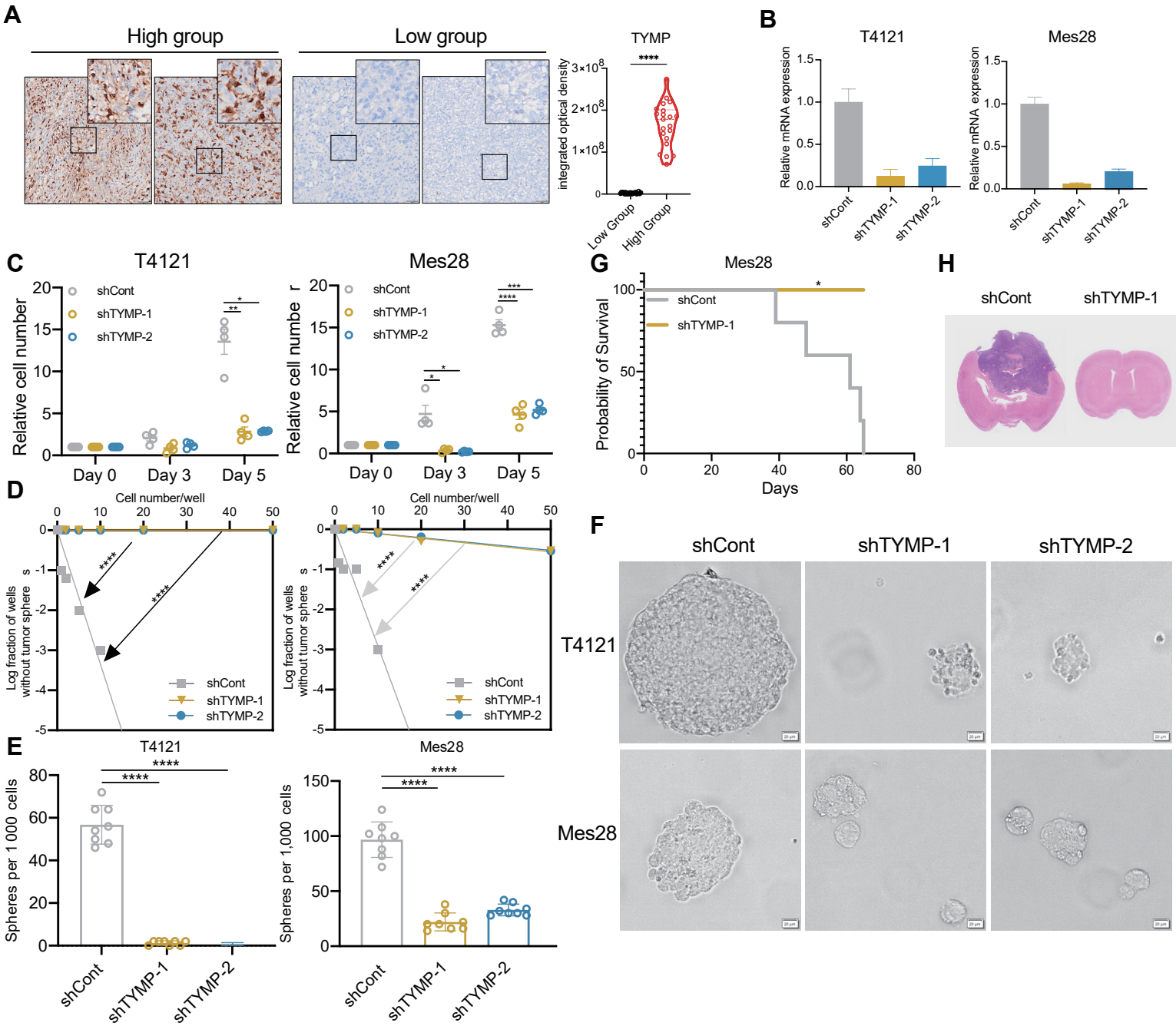
Figure S6

Figure S7



Supplementary figure legends

Figure S1. Glioma Sample Puncture for Proteomics Analyses

Representative histological area of either the tumor (T) or normal-appearing tissue (N) based on hematoxylin-eosin (H&E) staining slides are selected by two neuroscientists to ensure sample purity for punching. Areas of hemorrhagic, necrotic, or degenerative changes are excluded from puncture.

Figure S2. Quality Analysis for Proteomic Data

(A)-(B) Correlation analysis for mouse liver samples (A) which is the quality control for sample preparation and pool samples (B) which is the quality control for LC-MS/MS. (C) Violin plot shows that the technical replicates correlations index (Median = 0.93). (D)-(F) tSNE plots shows the variance among 27 batches, (D) three LC-MS/MS machines (E) and sample types (F).

Figure S3. Proteomics Differences Based on Clinical Classification

(A)-(C) tSNE plots shows the variance among tumor and normal-appearing sample types, (A) Sample types, (B) Four WHO grades of glioma, (C) Four histological types of glioma. (D) Heatmap shows 1893 differentially expressed proteins among four histological types of glioma (ANOVA test B-H adjusted $p < 0.001$), separated into two clusters, 987 proteins in cluster 1 and 1151 proteins in cluster 2. (F)-(G) Pathway enriched cluster 1 (F) and cluster 2 (G). (H)-(I) Metabolism associated network in cluster 1 (H) and cluster 2 (I).

Figure S4. Consensus Clustering for Proteomics Data

(A)-(D) The subgroups are identified based on proteomic data by K-means consensus clustering upon their abundance. k was tested from 2-6 and consensus matrices were shown of proteomic subtypes in (A) grade 1-4 glioma, (B) grade 1-3 glioma, (C) grade 4 glioma, and (D) IDH wildtype glioma.

Figure S5. Proteomic Classification in Different Subgroups

(A) Overall survival of different grade glioma patients in the study. (B)-(E) Heatmap and survival plots show the two subtypes classification in (B) grade 1-3 glioma patients, (C) grade 4 glioma patients, (D) IDH wildtype glioma patients.

Figure S6. Metabolism is Associated with Glioma Patients' Survival

(A) Patients' overall survival distribution of different glioma clinical classification. (B) Metabolism-related proteins screening process. (C) Overall survival of 18 metabolism-related proteins that closely associated with patients' prognosis.

Figure S7 TYMP is Required for GSC Proliferation and Self-renewal

(A) IHC validation of TYMP expression according to proteomic profiling. (B) TYMP mRNA levels in T4121 and Mes28 cells after knocking-down. (C) Proliferation assay shows targeting TYMP impairs the proliferation ability as assessed by cell number on day 3 and 5. (D) In vitro limiting dilution assays and (E) (F) tumorsphere formation shows the impairment of self-renewal of GSCs. The sphere number and size

significantly decreased in TYMP knockdown GSCs. (G)-(H) Knockdown of TYMP a significantly increased the survival of mouse. (K) HE staining of mouse brain shows the lack of TYMP inhibit growth of GSCs.