



(B) Patient summary of multimodal data.

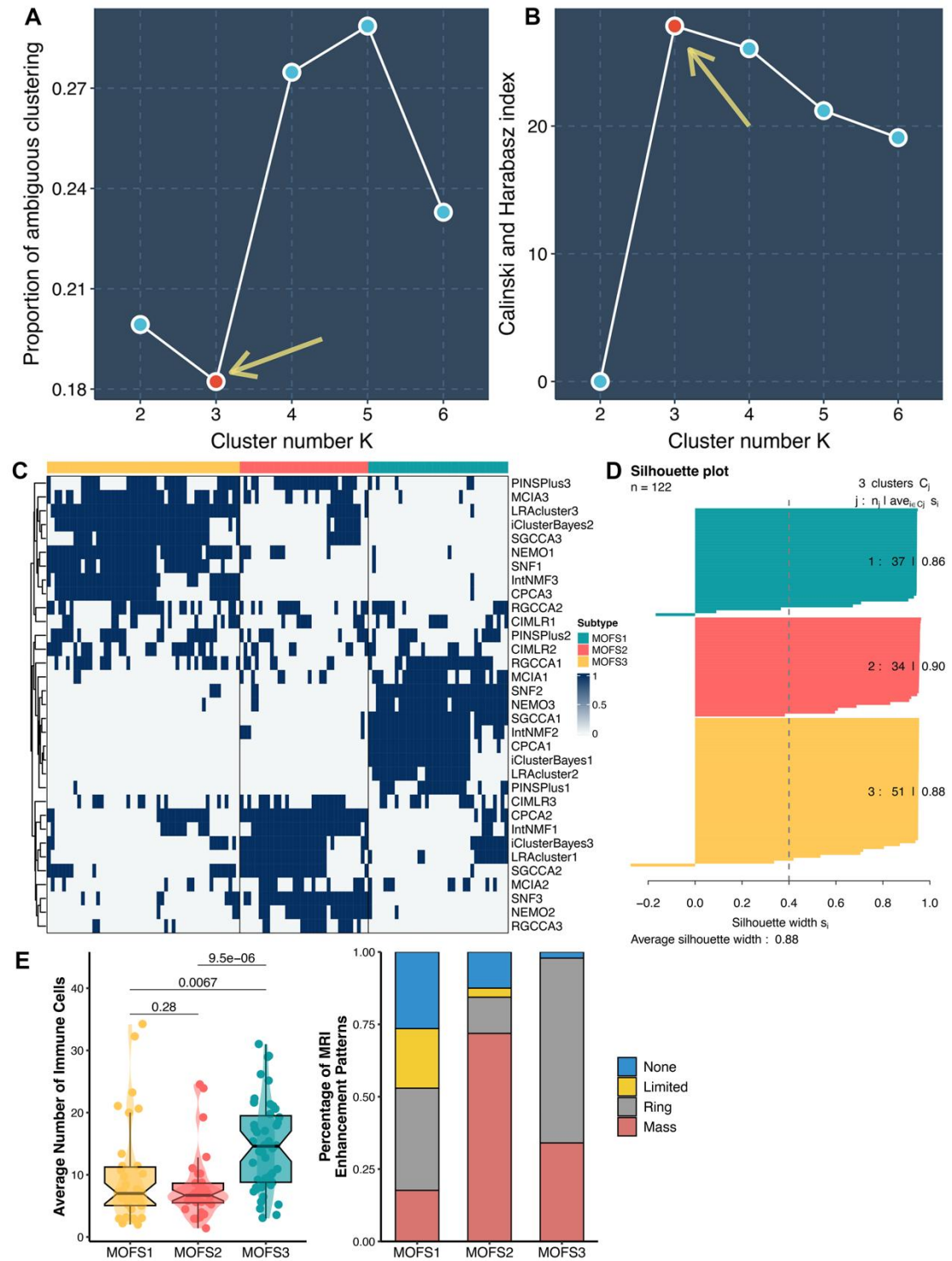


Figure S2 | Identification of Optimal Clustering Number and Radio-pathological Features.

(A) Proportion of ambiguous clustering (PAC) index for different cluster numbers, with $K = 3$ showing the lowest ambiguity.

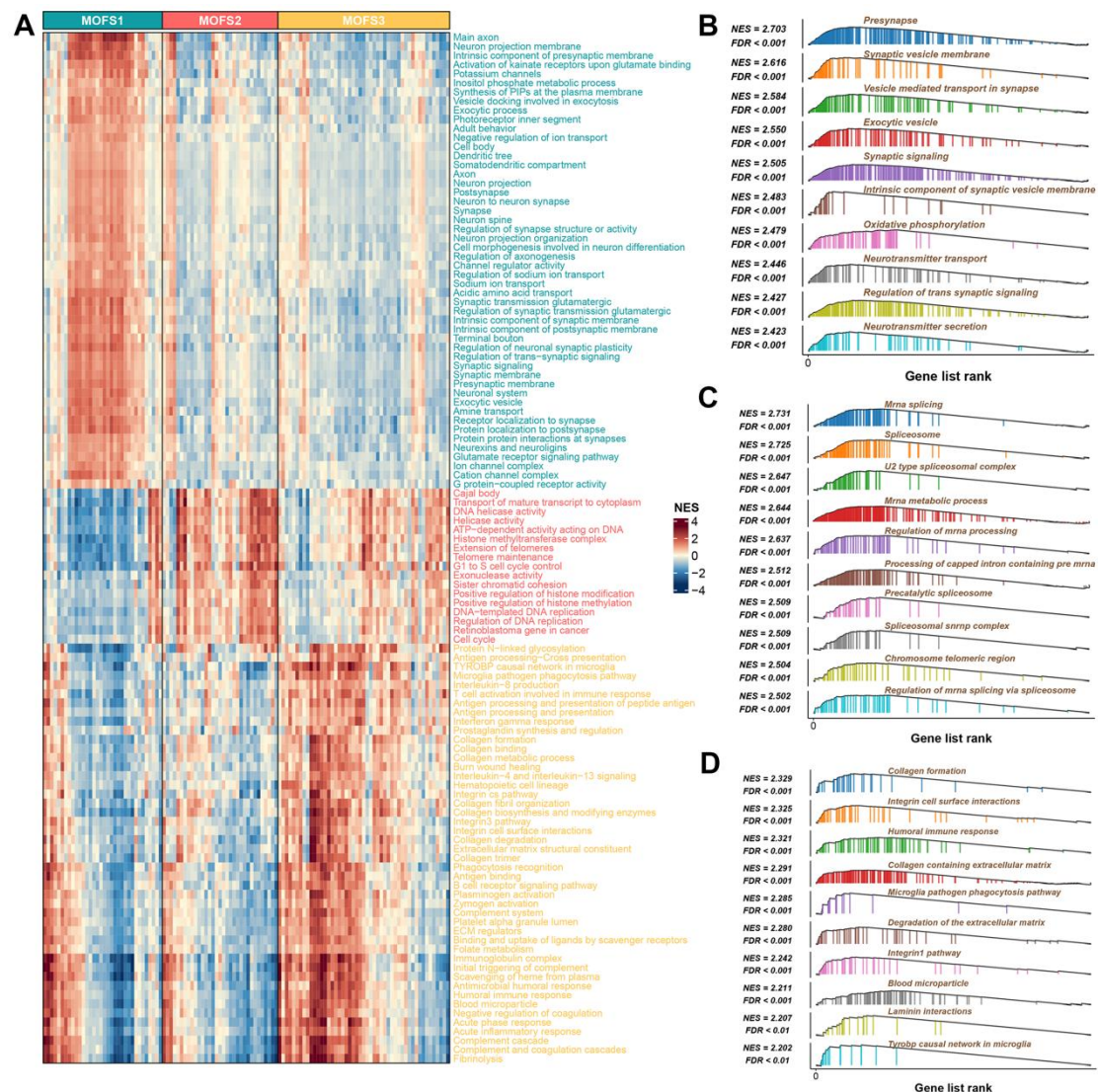
(B) Calinski and Harabasz index for different cluster numbers, with $K = 3$ achieving

the highest index value.

(C) Heatmap of consensus clustering results using 11 distinct intermediate fusion algorithms, demonstrating three distinct multimodal fusion subtypes (MOFS).

(D) Silhouette plot showing the distribution of silhouette coefficients under different clusters.

(E) Box plot showing the average number of immune cells per patch among MOFS subtypes; bar plot illustrating the percentage distribution of different MRI enhancement patterns (none, limited, ring, and mass) among MOFS1, MOFS2, and MOFS3 ($n = 116$). Statistic tests: Wilcoxon rank-sum test. Data are presented as box plots, with the center line representing the median, the box indicating the interquartile range (IQR, from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.



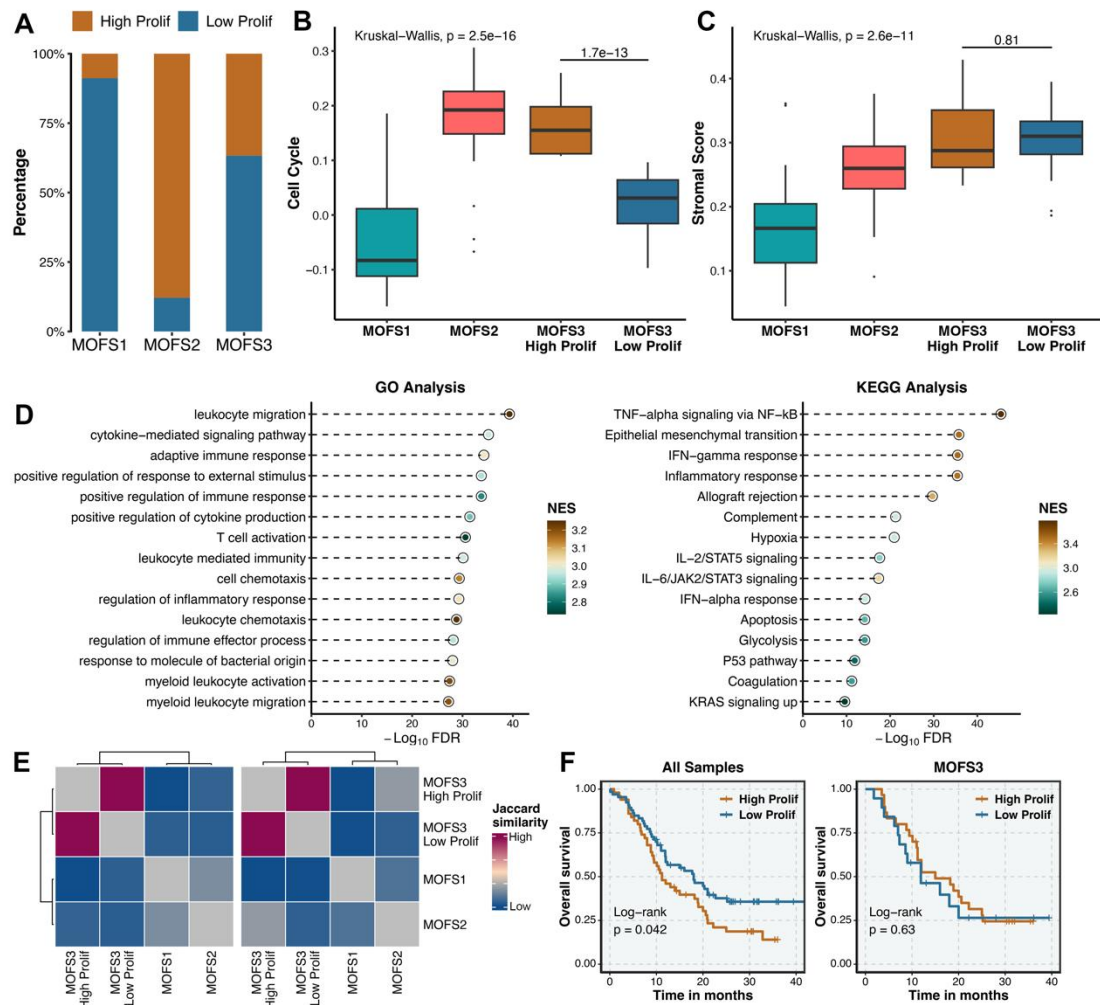


Figure S5 | Proliferation Heterogeneity within MOFS3 Samples.

(A) Proportion of high proliferation (High Prolif) and low proliferation (Low Prolif) samples in each MOFS subtype.

(B) Cell cycle scores across MOFS1, MOFS2, and MOFS3 proliferation subgroups ($n = 116$). Statistic tests: Kruskal-Wallis test and Wilcoxon rank-sum test. Data are presented as box plots, with the center line representing the median, the box indicating the interquartile range (IQR, from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.

(C) Stromal scores across MOFS1, MOFS2, and MOFS3 proliferation subgroups. MOFS3 has significantly higher stromal scores than MOFS1 and MOFS2, with no

difference between the high and low proliferation subgroups ($n = 116$). Statistic tests: Kruskal-Wallis test and Wilcoxon rank-sum test. Data are presented as box plots, with the center line representing the median, the box indicating the interquartile range (IQR, from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.

(D) GO and KEGG pathway enrichment of upregulated genes in MOFS3 High Prolif versus MOFS2. MOFS3 High Prolif samples remain enriched in TME-related pathways, retaining the TME-rich identity of MOFS3.

(E) Jaccard similarity heatmaps for upregulated (left) and downregulated (right) gene sets. MOFS3 High Prolif and Low Prolif groups show the highest similarity.

(F) Kaplan-Meier survival curves for high and low proliferation groups. High proliferation predicts worse prognosis in the overall cohort ($n = 116$, $P = 0.042$) but not within MOFS3 ($n = 49$, $P = 0.63$). Statistic tests: log-rank test.

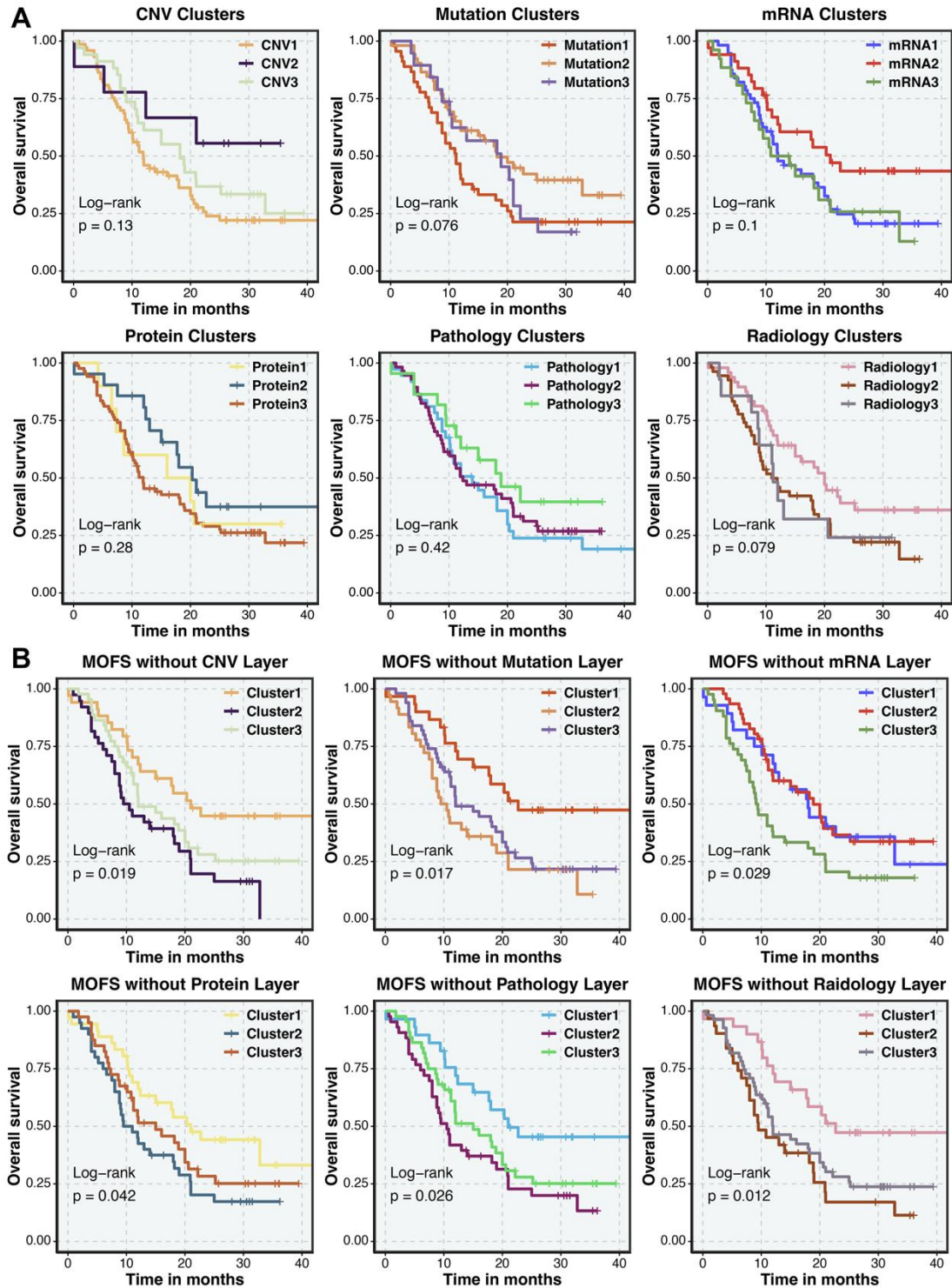


Figure S6 | Effect of individual modalities on survival analysis.

(A) Kaplan-Meier survival curves for clusters derived from individual modalities ($n = 116$). Statistic tests: log-rank test.

(B) Kaplan-Meier survival curves for clusters obtained by excluding specific

modalities ($n = 116$). Statistic tests: log-rank test.

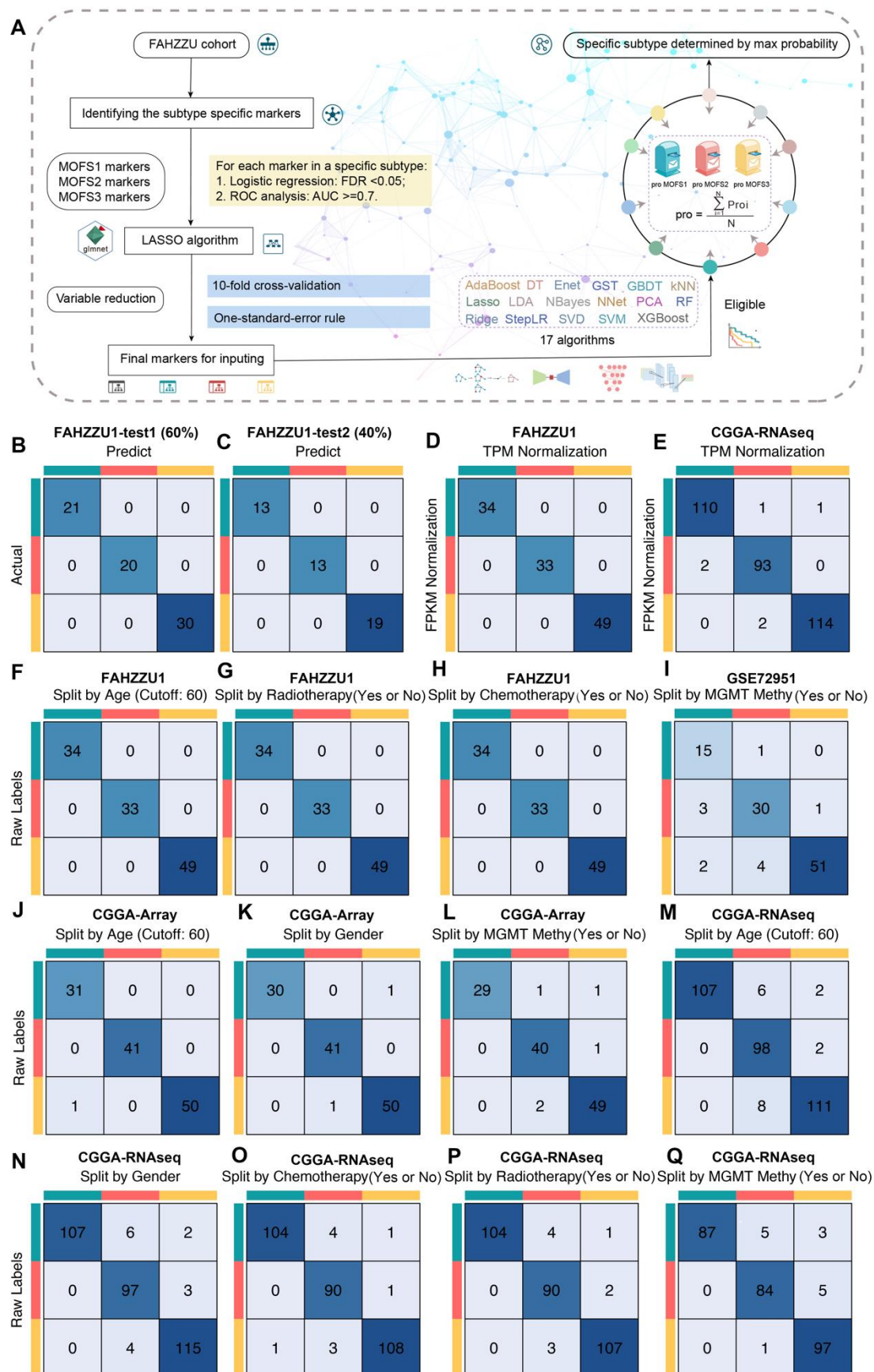


Figure S7 | Development and Evaluation of the MOFS Ensemble Classifier.

(A) The schematic representation of the MOFS ensemble classifier.

(B-C) Performance of the classifier on FAHZZU1-test1 (60% random split) and FAHZZU1-test2 (40% random split) subsets.

(D-E) Confusion matrices for FAHZZU1 and CGGA-RNAseq cohorts, showing the classifier's robustness to different RNA normalization methods.

(F-H) Stratified analysis of FAHZZU1 cohort by age (cutoff: 60 years), radiotherapy (Yes/No), and chemotherapy (Yes/No).

(I) Stratified analysis of the GSE72951 data by MGMT methylation status.

(J-L) Stratified analysis of the CGGA-Array cohort by age (cutoff: 60 years), gender, and MGMT methylation status.

(M-Q) Stratified analysis of the CGGA-RNAseq cohort by age (cutoff: 60 years), gender, chemotherapy (Yes/No), radiotherapy (Yes/No), and MGMT methylation status.

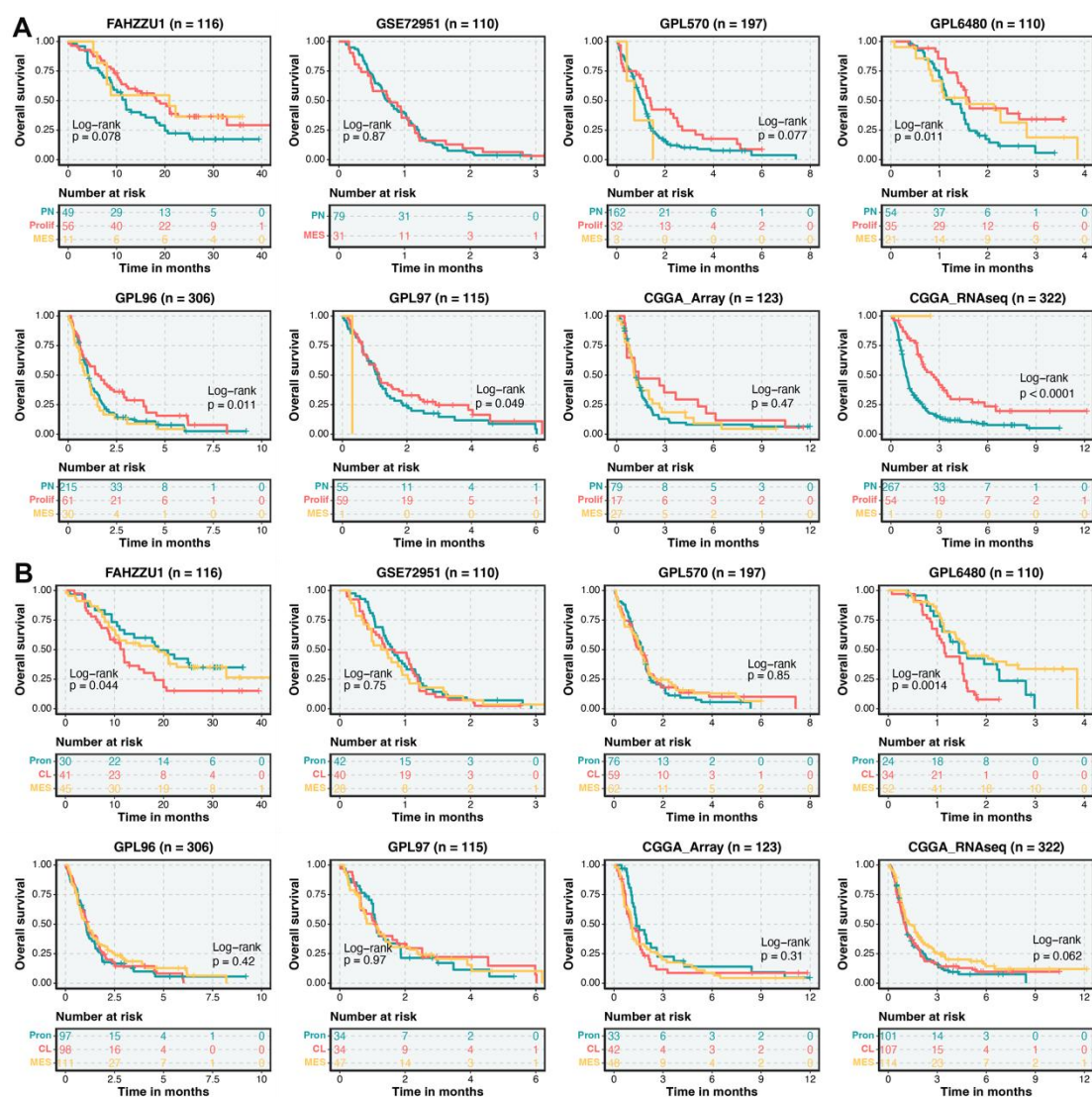


Figure S8 | Prognostic Analysis of Phillips and Wang Classifications.

(A) Kaplan-Meier survival analysis of the Phillips classification. Statistic tests: log-rank test.

(B) Kaplan-Meier survival analysis of the Wang classification. Statistic tests: log-rank test.

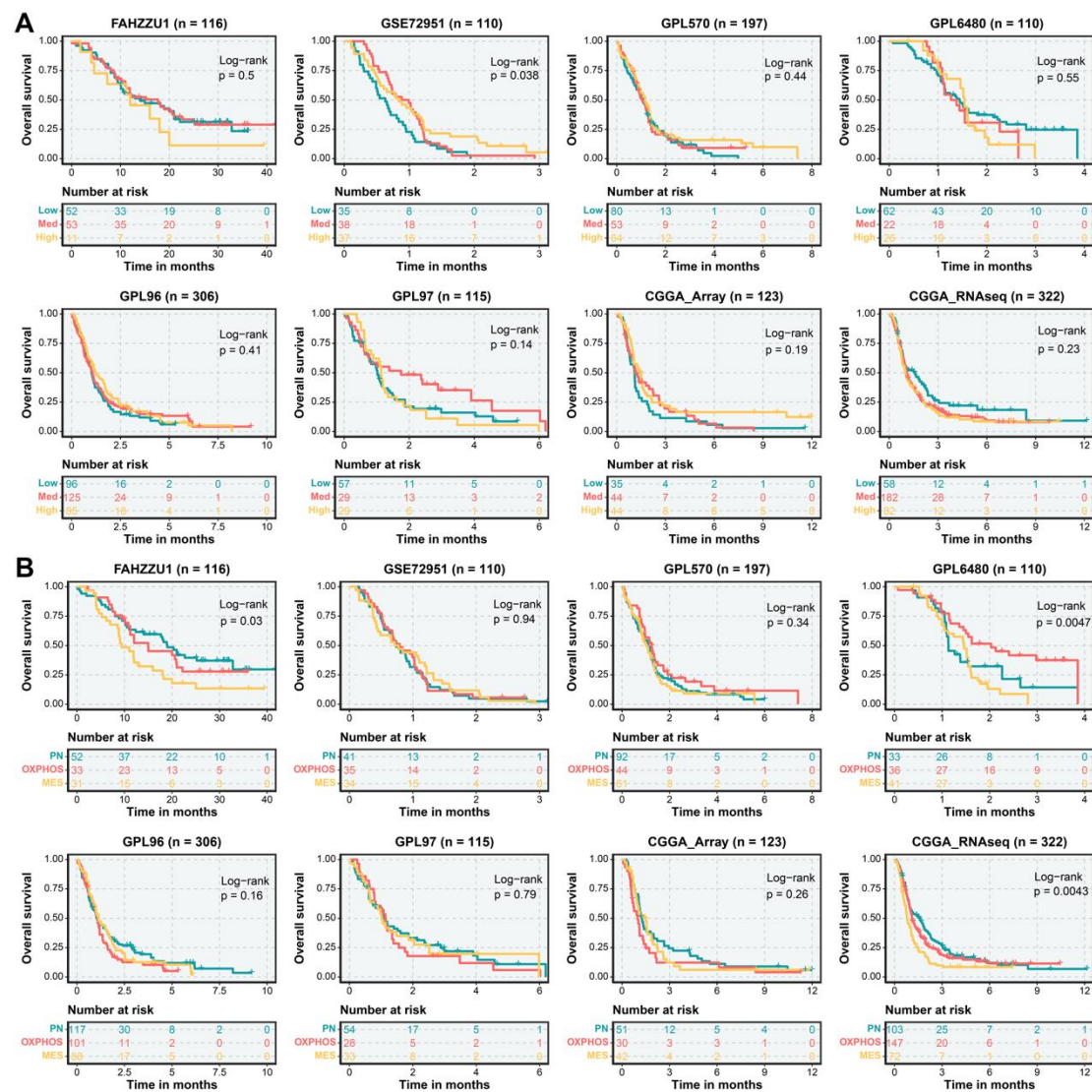


Figure S9 | Prognostic Analysis of White and Wu Classifications.

(A) Kaplan-Meier survival analysis of the White classification. Statistic tests: log-rank test.

(B) Kaplan-Meier survival analysis of the Wu classification. Statistic tests: log-rank test.

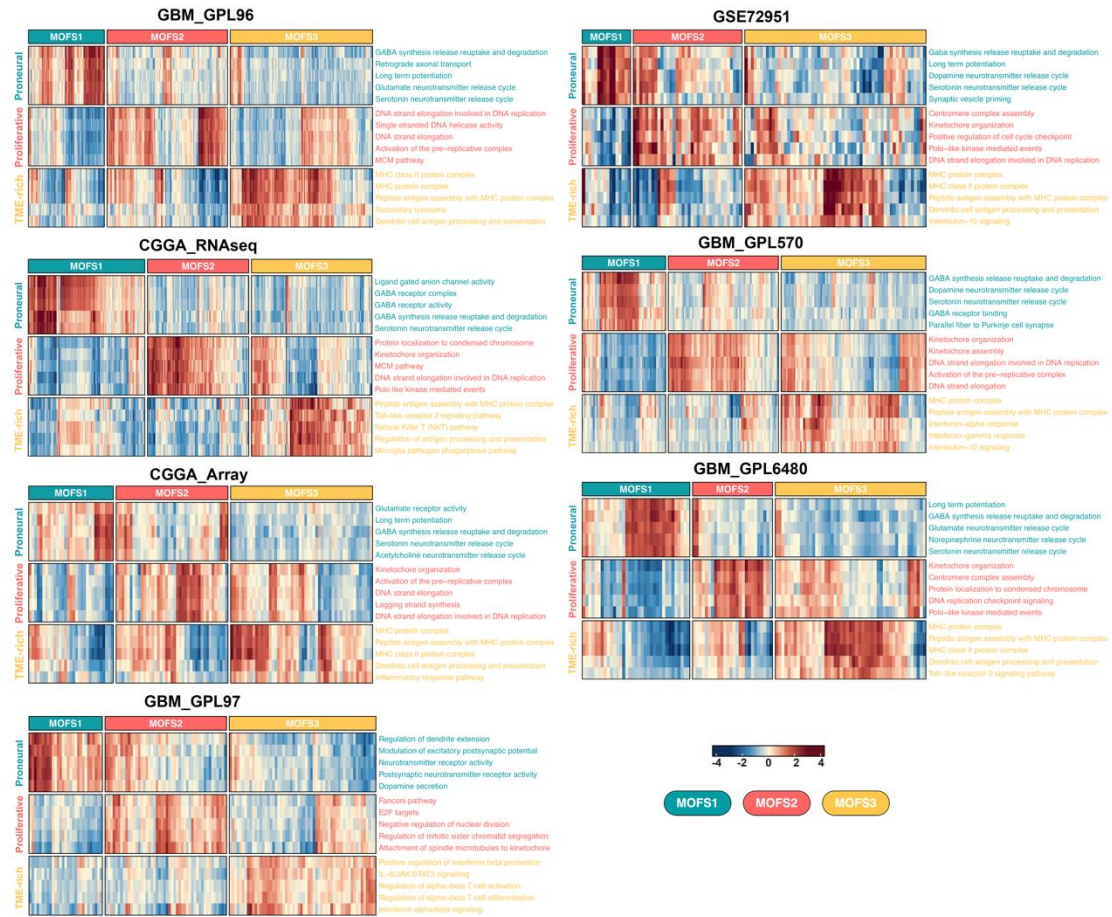


Figure S10 | Functional Validation of MOFS Subtypes

Heatmaps displaying enrichment scores for individual pathways across MOFS subtypes in seven external cohorts. The heatmaps illustrate consistent biological attributes for MOFS subtypes (proneural, proliferative, and TME-rich) across different datasets, confirming the stability and robustness of the MOFS classification.

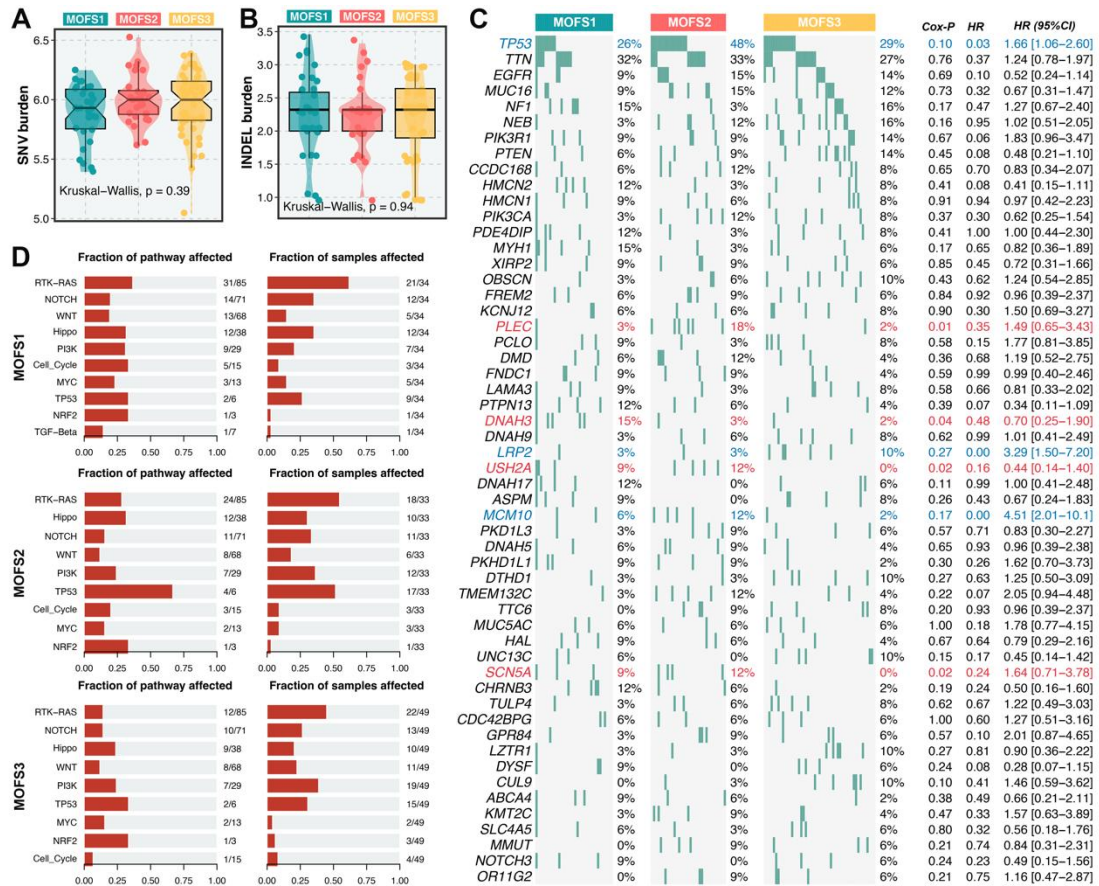


Figure S11 | Genomic Alteration Characteristics of MOFS Subtypes.

(A) Single nucleotide variation (SNV) burden across MOFS subtypes, showing no significant differences ($n = 116$). Statistic tests: Kruskal-Wallis test. Data are presented as box plots, with the center line representing the median, the box indicating the interquartile range (IQR, from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.

(B) Insertions/deletions (INDELs) burden across MOFS subtypes, indicating no significant differences ($n = 116$). Statistic tests: Kruskal-Wallis test. Data are presented as box plots, with the center line representing the median, the box indicating the IQR (from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.

(C) Heatmap of significant mutation differences among MOFS subtypes, highlighting mutations in TP53, LRP2, and MCM10 associated with unfavorable prognosis, and specific mutations in SCN5, USH2A, PLEC, and DNAH3 (n = 116). Statistical tests: Likelihood ratio test.

(D) Fraction of pathways and samples affected by mutations in 10 canonical pathways across MOFS subtypes.

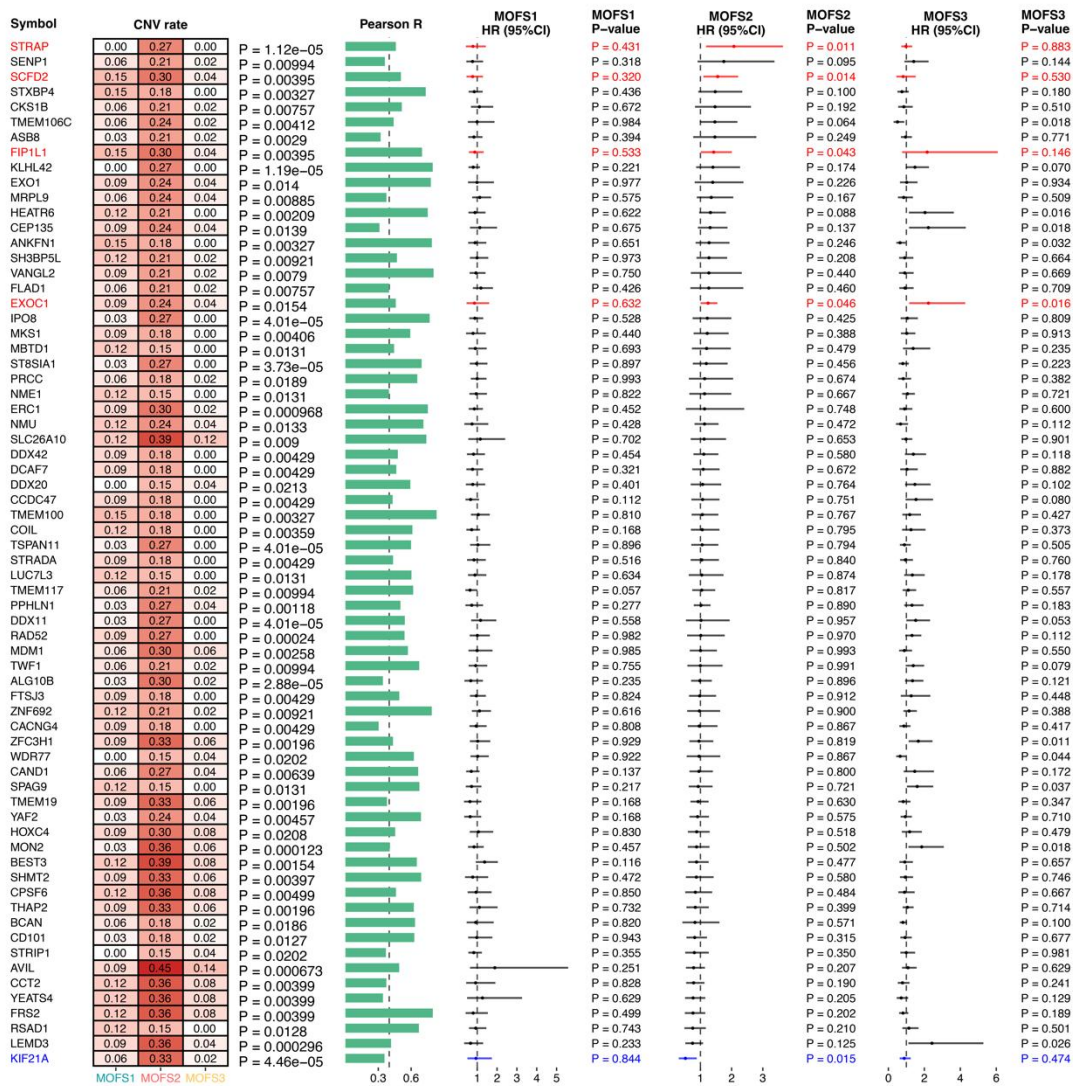


Figure S12 | CNV Analysis for MOFS Subtypes.

Heatmap showing the CNV rates of significant genes across MOFS subtypes, with Pearson correlation coefficients indicating the strength of association between CNV

and gene expression. Forest plot of Cox regression analysis identifying STRAP, SCFD2, FIP1L1, and EXOC1 as risk factors in MOFS2, and KIF21A as a protective factor ($n = 116$). Statistic tests: Fisher test and Likelihood ratio test.

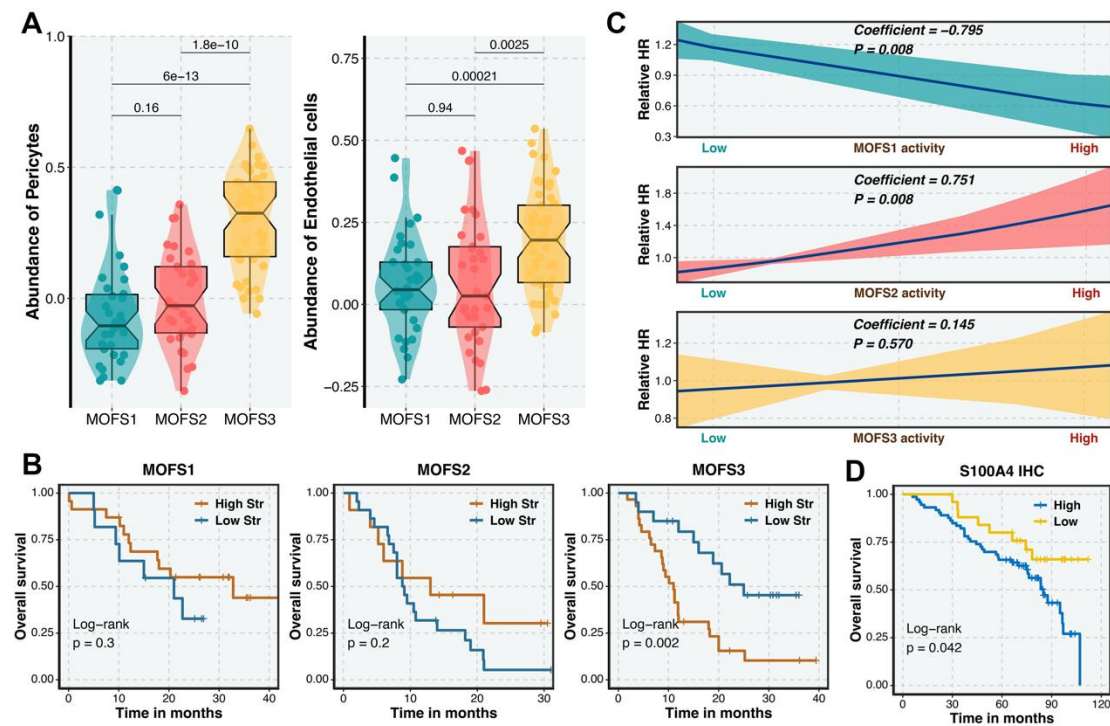


Figure S13 | Stromal Infiltration and Prognostic Significance in MOFS Subtypes.

(A) Infiltration abundance of endothelial cells and pericytes across MOFS subtypes ($n = 116$). Statistic tests: Wilcoxon rank-sum test. Data are presented as box plots, with the center line representing the median, the box indicating the interquartile range (IQR, from the 25th to the 75th percentile), and the whiskers extending to the most extreme data points within 1.5 times the IQR; points beyond this range are shown as individual outliers.

(B) Kaplan-Meier survival curves for MOFS subtypes stratified by stromal cell abundance, demonstrating significant prognostic differences in MOFS3 ($n = 116$). Statistic tests: log-rank test.

(C) Cox regression analysis indicating MOFS1 score is associated with better

prognosis, MOFS2 score with worse prognosis, and MOFS3 score not statistically significant (n = 116). Statistic tests: Likelihood ratio test.

(D) Kaplan-Meier survival analysis of the tissue microarray (TMA) results, confirming the association between high levels of S100A4 and worse prognosis (n = 98). Statistic tests: log-rank test.

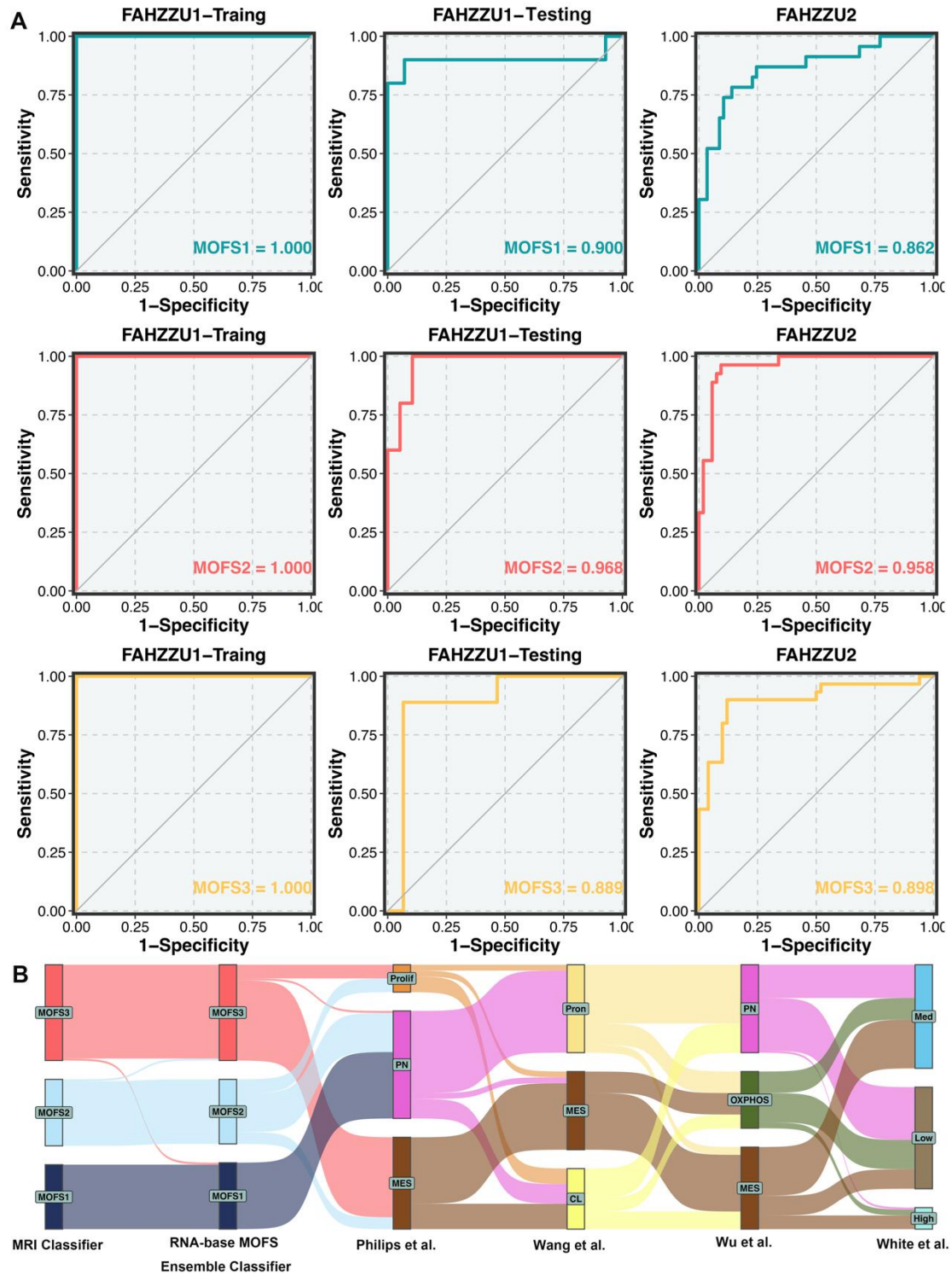


Figure S14 | ROC Curves for DNN Model and Multi-Classifier Comparison.

(A) Receiver operating characteristic (ROC) curves showing the performance of the deep neural network (DNN) model in predicting MOFS subtypes across different datasets. The model achieved an area under the curve (AUC) of 1.000 for each MOFS subtype on the FAHZZU1 training set, 0.900, 0.968, and 0.889 on the FAHZZU1

testing set, and 0.862, 0.958, and 0.898 on the FAHZZU2 cohort for MOFS1, MOFS2, and MOFS3, respectively. The high AUC values indicate the model's accuracy and stability in predicting MOFS subtypes.

(B) The Sankey diagram illustrates the relationships between classifications derived from the MRI classifier, the RNA-based MOFS ensemble classifier, and traditional glioma classification systems, including Phillips et al. (2006), Wang et al. (2018), Wu et al. (2024), and White et al. (2023). The leftmost column represents the MOFS subtypes (MOFS1, MOFS2, MOFS3) predicted by the MRI classifier. The second column corresponds to MOFS subtypes derived from the RNA-based MOFS ensemble classifier. The subsequent columns represent classifications based on Phillips' proneural (PN), proliferative (Prolif), and mesenchymal (MES) subtypes; Wang's proneural (PN), classical (CL), and mesenchymal (MES) subtypes; Wu's oxidative phosphorylation (OXPHOS) and mesenchymal (MES) subtypes; and White's low, medium, and high TME subtypes. The width of the bands indicates the proportion of samples shared between classifications.