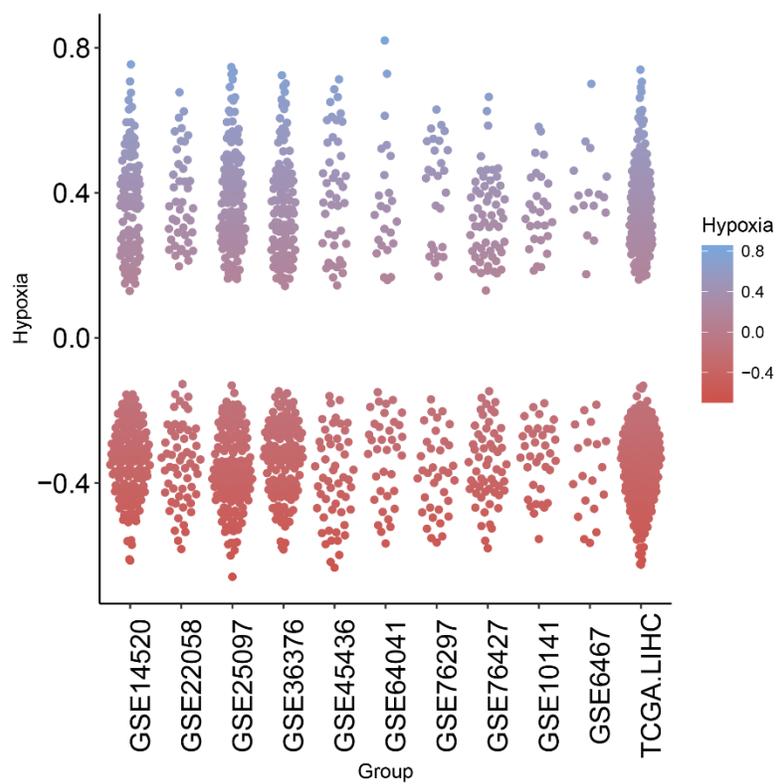
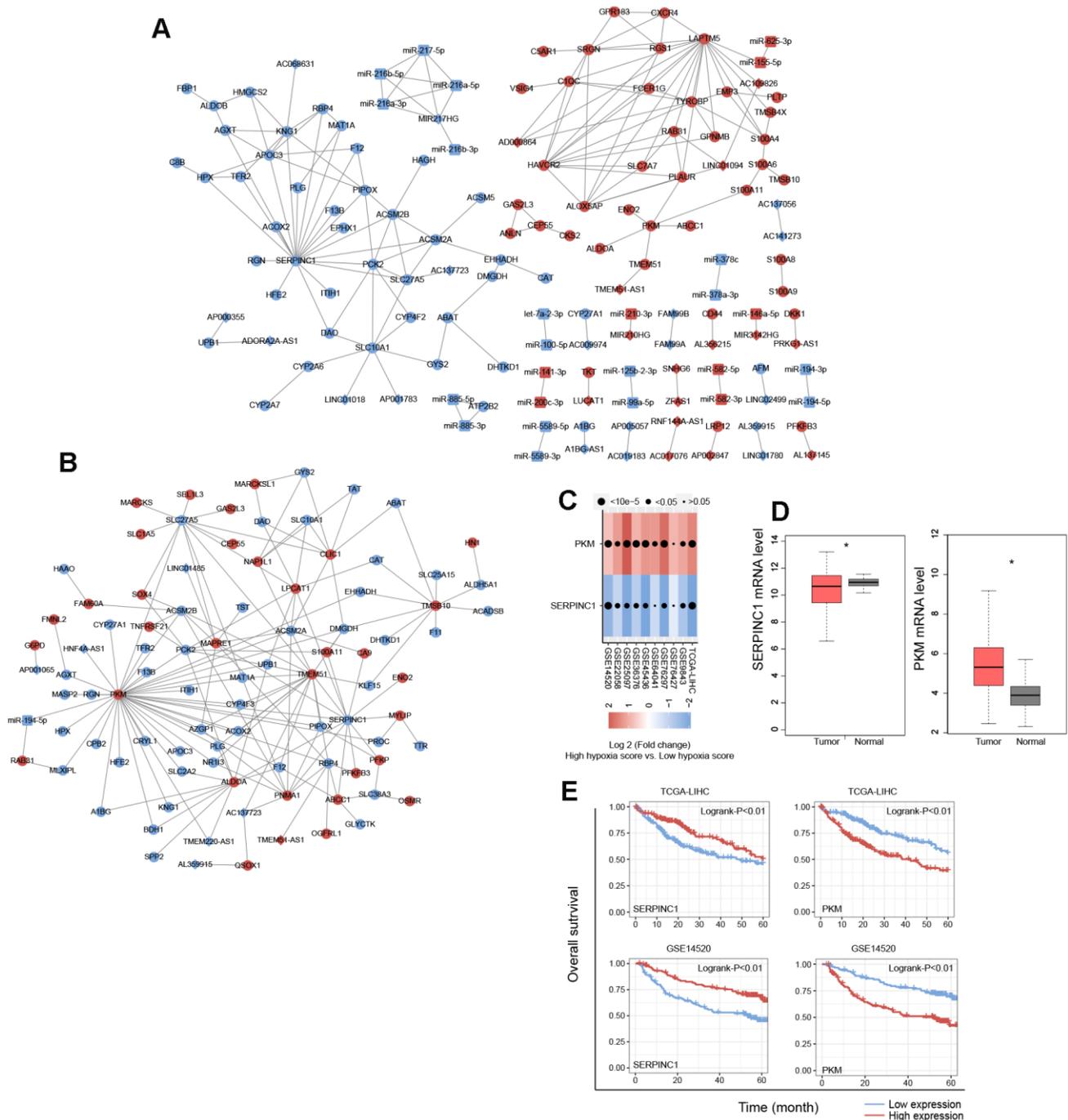


## SUPPLEMENTARY FIGURES



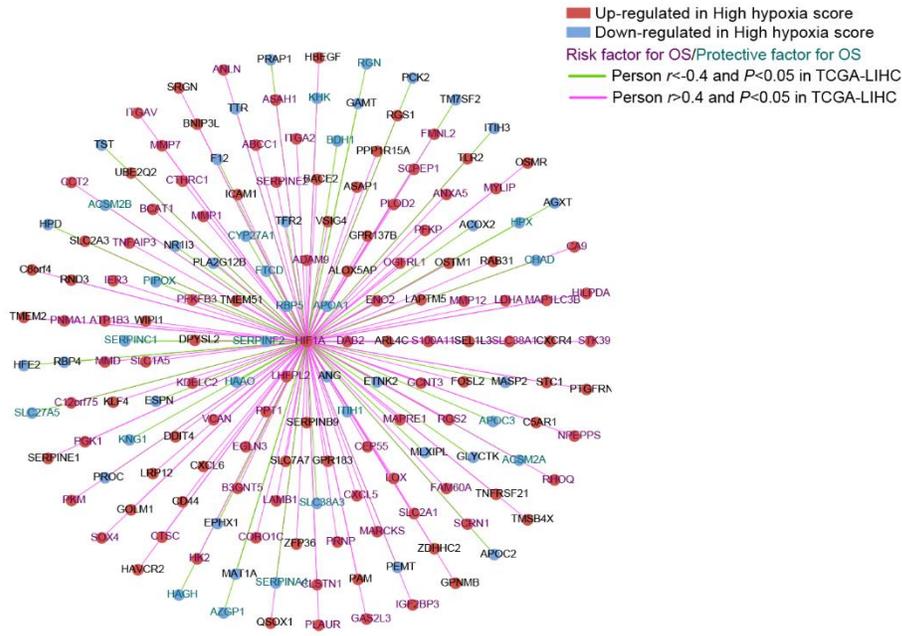
Supplementary Figure 1. The distribution of hypoxia scores calculated based on the 21-gene hypoxia signature in the cancer tissues of 11 HCC cohorts.



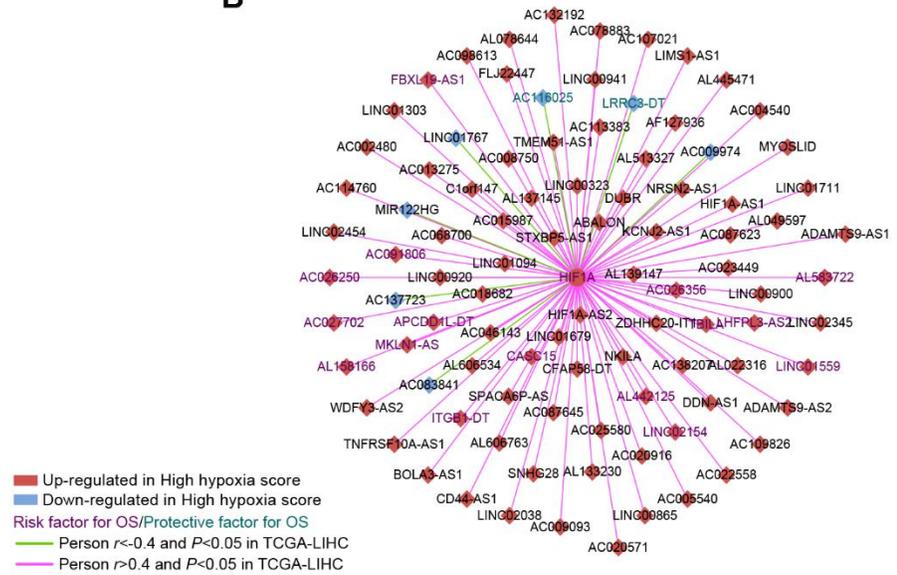


**Supplementary Figure 3. A co-expression network formed by HF/DE-mRNAs, DE-miRs, and DE-lncRNAs. (A, B)** The correlations among HF/DE-mRNAs, DE-miRs, and DE-lncRNAs were obtained using Pearson correlation analysis. The nodes with  $|Pearson\ r| > 0.8$  and  $P < 0.05$  constitute positive and negative co-expression networks. **(C)** In the positive and negative co-expression networks, the 2 genes with the highest connectivity are SERPINC1 and PKM. Their differences among 10 hepatocellular carcinomas (HCC) datasets are shown in the heat map. **(D)** Differences in the expression of SERPINC1 and PKM between normal tissues and cancer tissues of HCC patients in TCGA-LIHC. **(E)** SERPINC1 and PKM are associated with patient survival in TCGA-LIHC and GSE14520.

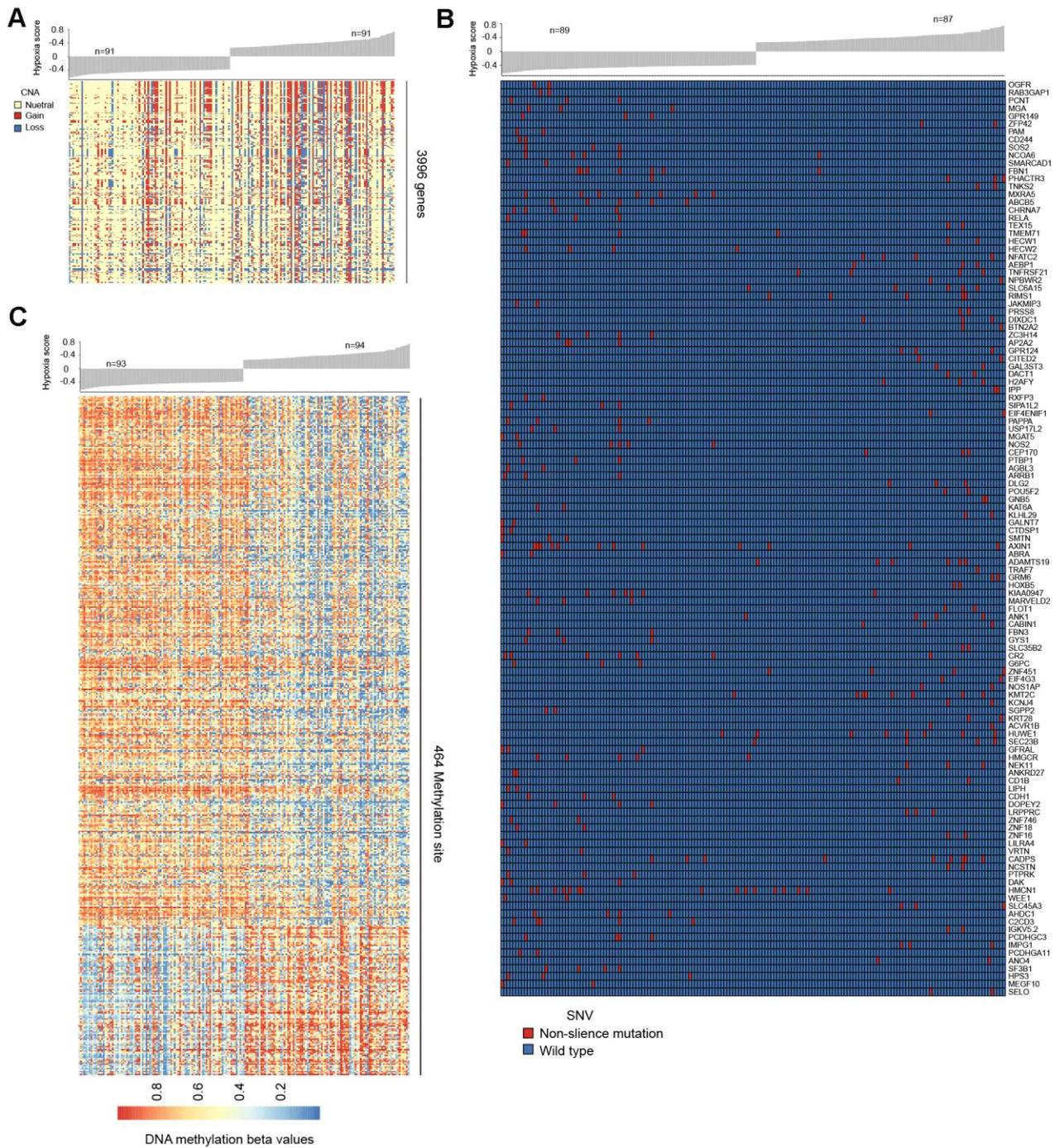
A



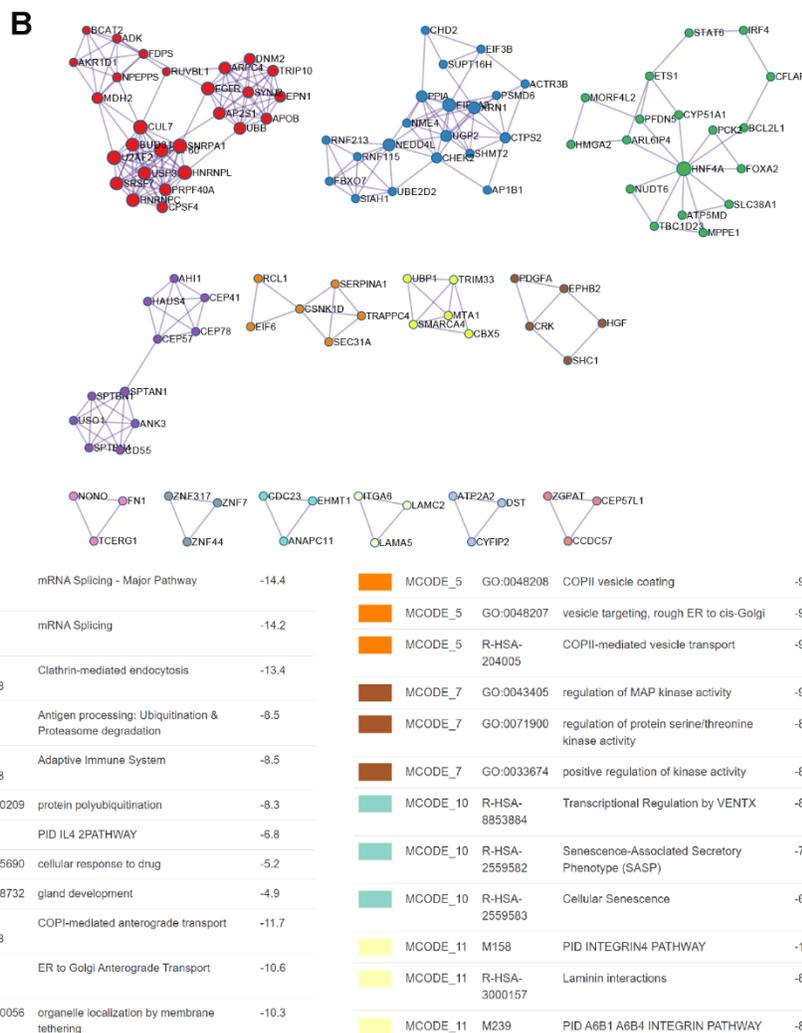
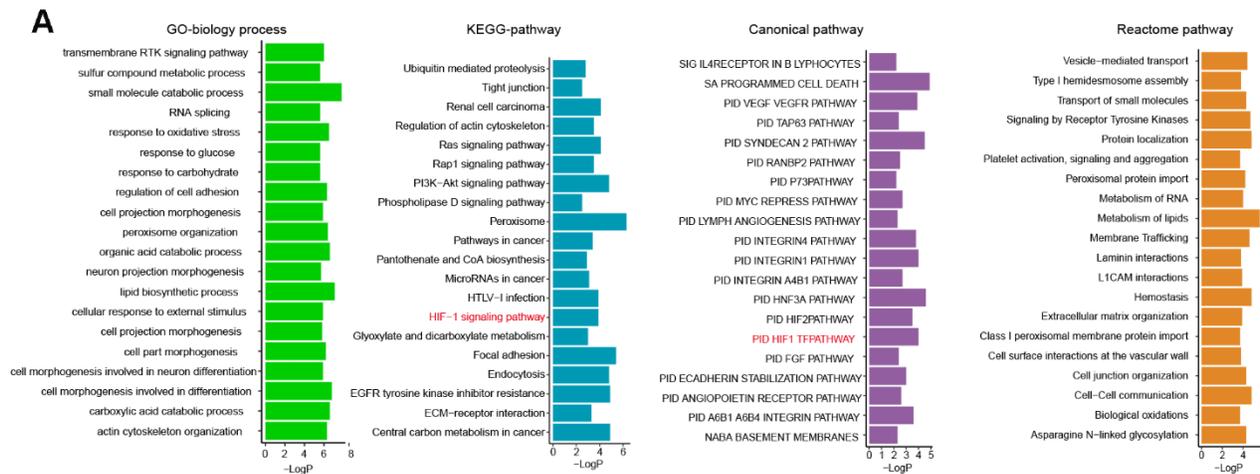
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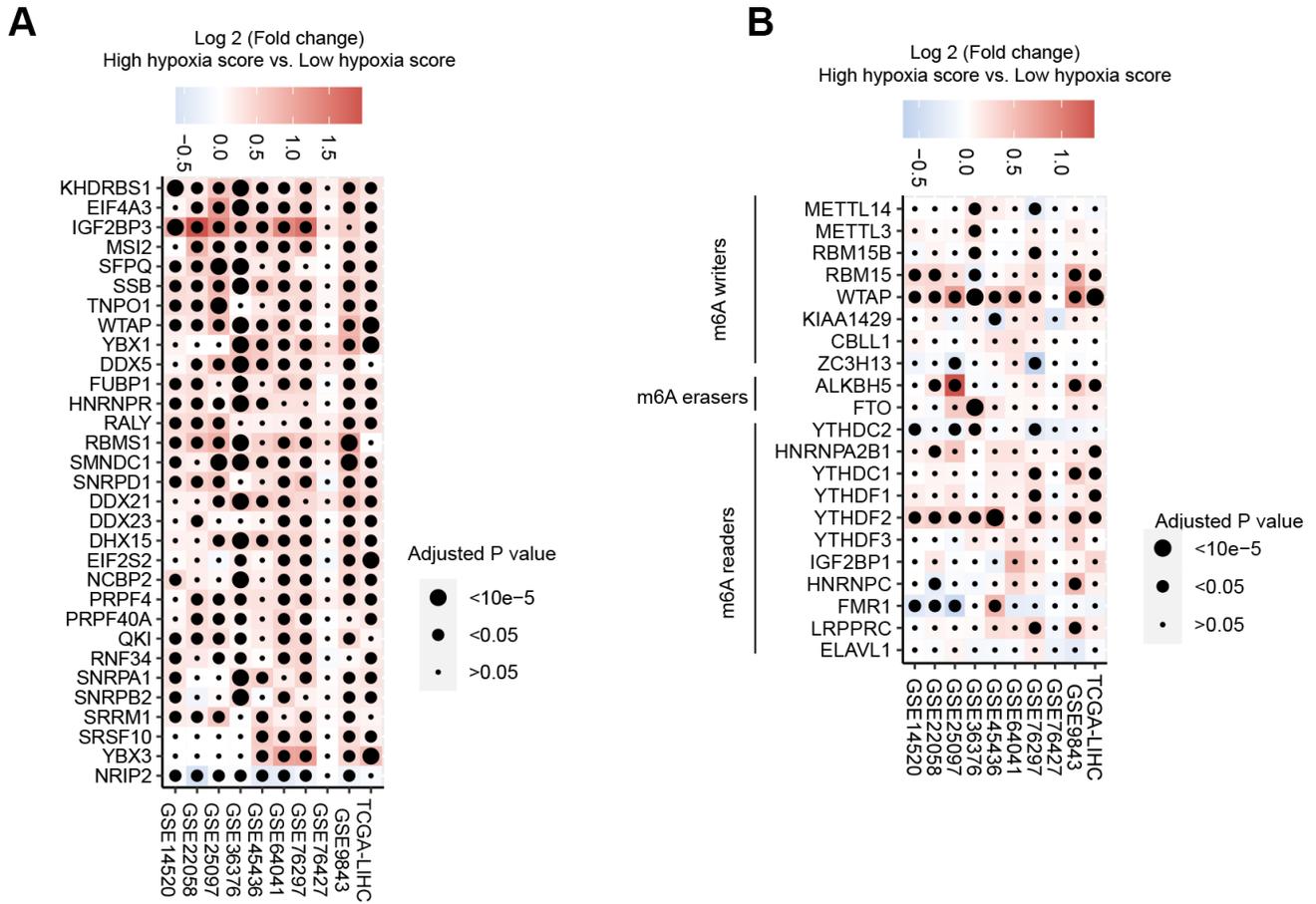
**Supplementary Figure 4. DE-mRNAs and DE-lncRNAs correlated with hypoxia-inducible factor 1-alpha (HIF-1A) mRNA.** The correlations were calculated by Pearson correlation analysis using TCGA-LIHC data. (A) DE-mRNAs correlated with HIF-1A mRNA. (B) DE-lncRNAs correlated with HIF-1A mRNA.



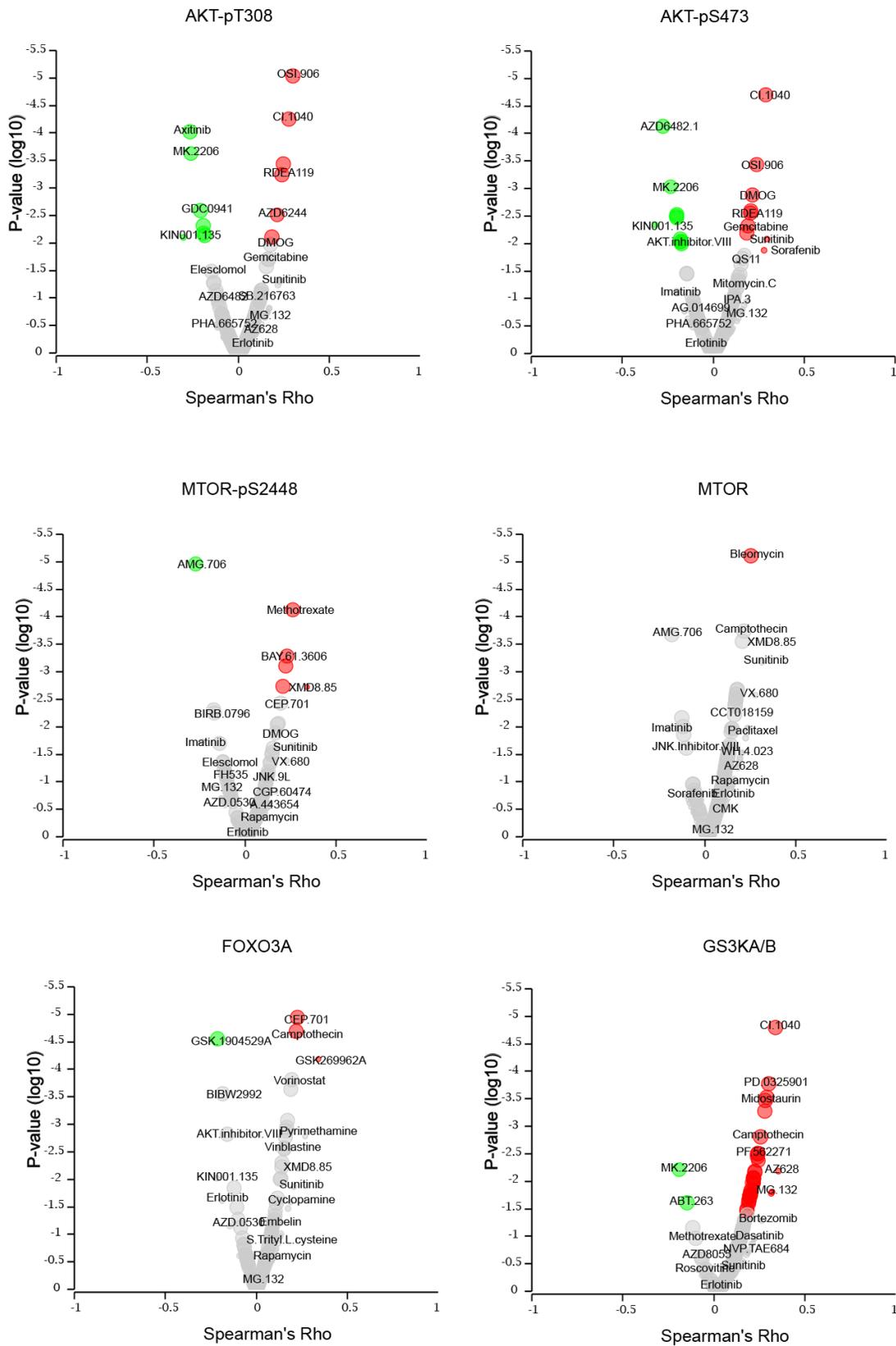
**Supplementary Figure 5. Overview of genomic alterations and DNA methylation changes in groups with high hypoxia scores and low hypoxia scores.** (A) Difference in the proportions of copy-number aberrations (CNAs) between the high hypoxia score group and the low hypoxia score group. (B) Proportions of single-nucleotide variants (SNVs) in 172 genes distributed in the low hypoxia score group and the high hypoxia score group. (C) A total of 464 loci with different methylation levels in the high hypoxia score group and the low hypoxia score group.



**Supplementary Figure 6. Functional enrichment analysis of biological processes and pathways for 681 mRNAs involving differential AS events.** (A) A total of 681 mRNAs are involved in AS events with differences in occurrences between the high hypoxia score group and the low hypoxia score group. The top 20 (sorted by P-value) enrichment analysis results for GO biological processes and enrichment analysis results for pathways from 3 different data sources are displayed. (B) The protein-protein interaction (PPI) enrichment network of the translation products of the 681 mRNAs were constructed using the MCODE algorithm.



**Supplementary Figure 7. The expression of 30 splicing factors and 21 N6-methyladenosine (m6A) regulators in the high hypoxia score group and the low hypoxia score group. (A)** Differences in the expression of 30 splicing factors between the high hypoxia score groups and the low hypoxia score groups in 10 HCC datasets. **(B)** Differences in the expression of 21 m6A regulators between the high hypoxia score groups and the low hypoxia score groups in 10 HCC datasets.



**Supplementary Figure 8. Spearman's correlation coefficients for proteins with significantly different expression in the high hypoxia score group and the low hypoxia score group and commonly used anticancer drugs.** The data were obtained from the MD Anderson Cell Lines Project and the Genomics of Drug Sensitivity in Cancer database.