Glioblastoma Stem Cells: MAP17 as a Novel Predictive Biomarker and Therapeutic Target Associated with Quiescence and Immune Evasion

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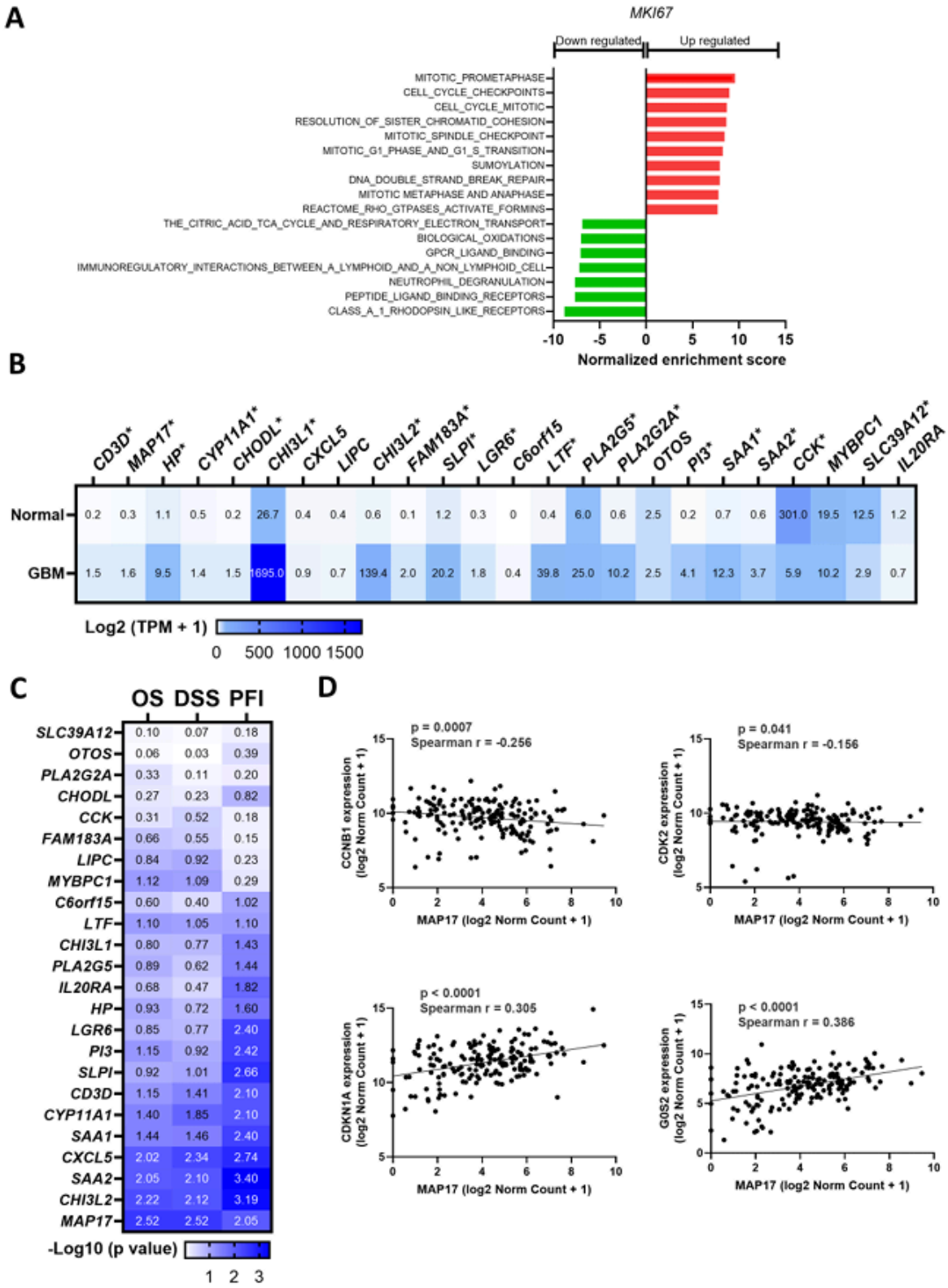
Expertise

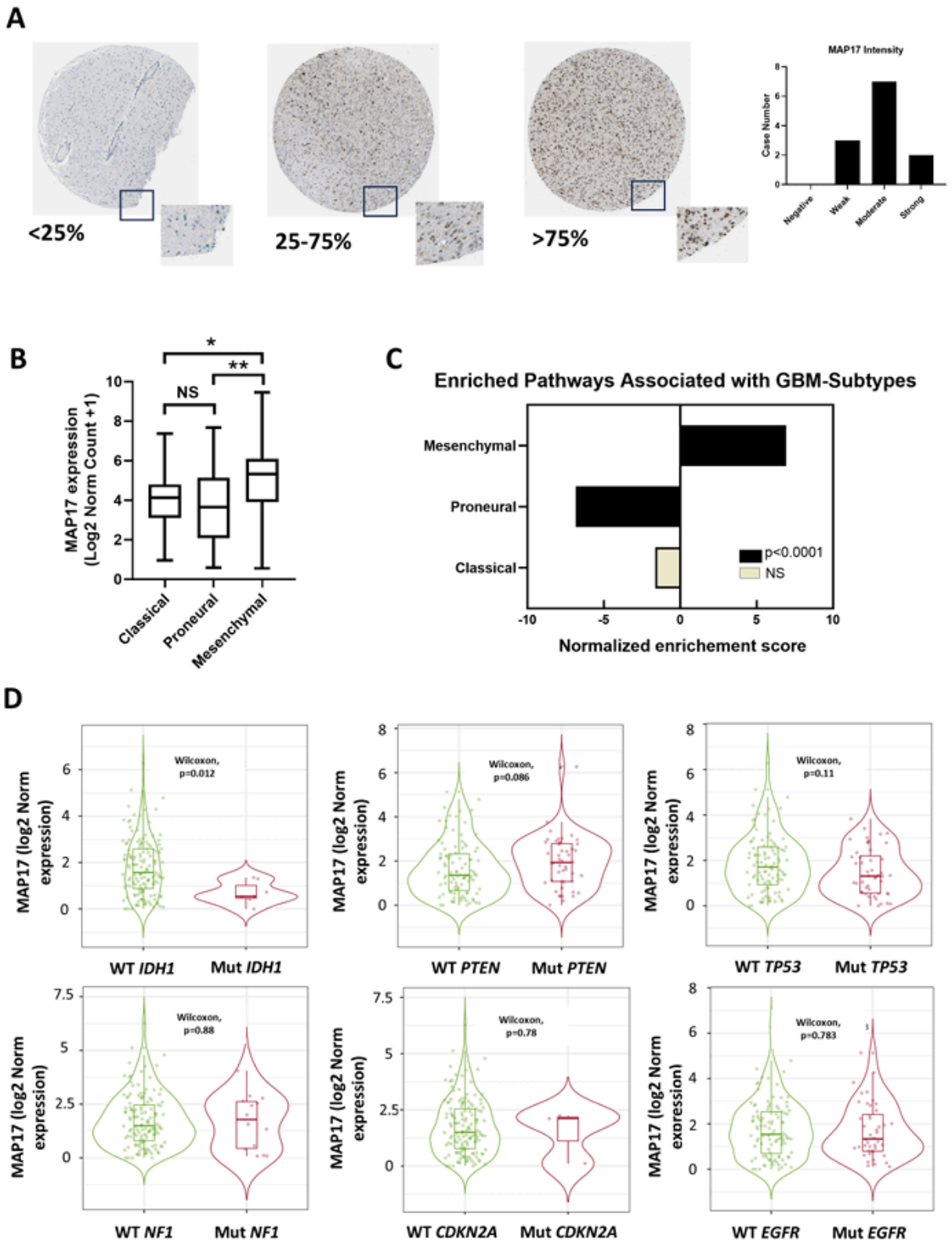
Bioinformatics and Programming: Developed automated pipelines using Python and Docker to process bulk RNA-seq and proteomics data. Leveraged bioinformatics tools (e.g., UCSC Xena, GEPIA, TIMER 2.0) for differential gene expression analysis and immune profiling.
Biomarker Discovery: Identified MAP17 as a novel glioblastoma biomarker through pathway enrichment and correlation with quiescence, immune evasion, and metabolic pathways. Conducted survival analyses and immune checkpoint evaluations to validate its clinical significance.
Data Analysis and Visualization: Applied advanced statistical modeling and visualization techniques to uncover immune microenvironment dynamics. Created intuitive visualizations (heatmaps, bubble plots, bar graphs) to communicate findings effectively.
Computational Modeling: Modeled metabolic pathways (e.g., folate, zinc, fatty acids) linked to glioblastoma stem cell phenotypes. Simulated metabolic and immune interactions to reveal therapeutic vulnerabilities in therapy-resistant clones.
AI Integration: Used machine-readable datasets and AI-driven approaches to predict immune dynamics and model tumor-immune interactions, laying a foundation for personalized medicine applications.

Impact of Results

- Identified MAP17 as a novel therapeutic biomarker and target in glioblastoma, revealing its role in promoting quiescence, stemness, and immune evasion.
- Advanced understanding of the glioblastoma immune microenvironment by uncovering correlations between MAP17 and immune checkpoint inhibitors, supporting precision oncology.
- Highlighted metabolic reprogramming in therapy-resistant glioblastoma stem cells, identifying potential pathways for targeted interventions.
- Enhanced reproducibility and scalability of omics data analyses, ensuring high-quality insights for guiding drug development and biomarker validation.
- Demonstrated the potential of AI and computational modeling to integrate multi-omics data, accelerating discoveries across diseases and biological systems.



Identification of Membrane-Associated Protein 17 (MAP17) as a potential biomarker in non-proliferative glioblastoma multiforme (GBM).

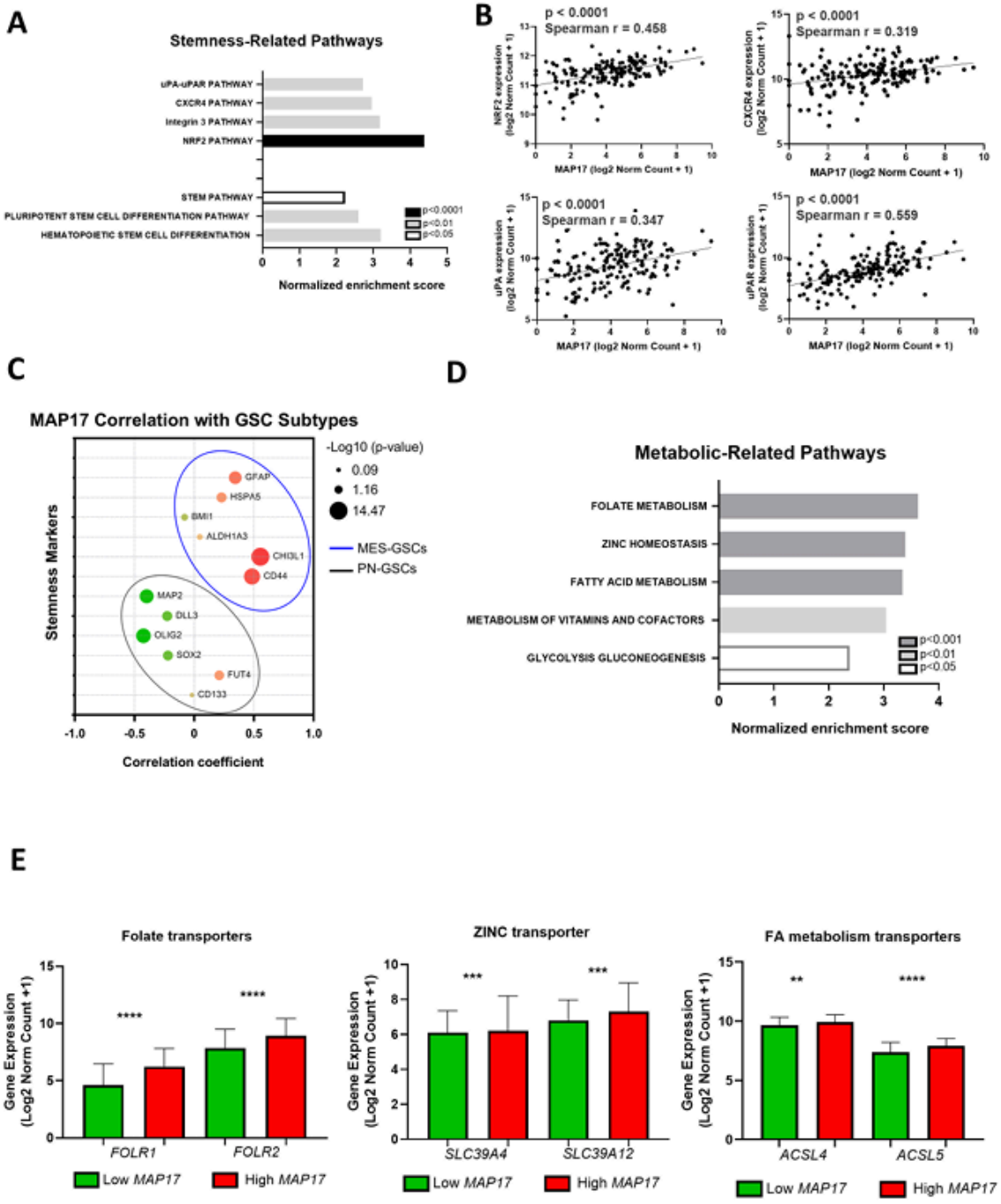


Histopathology and clinical relevance of MAP17inGBM.

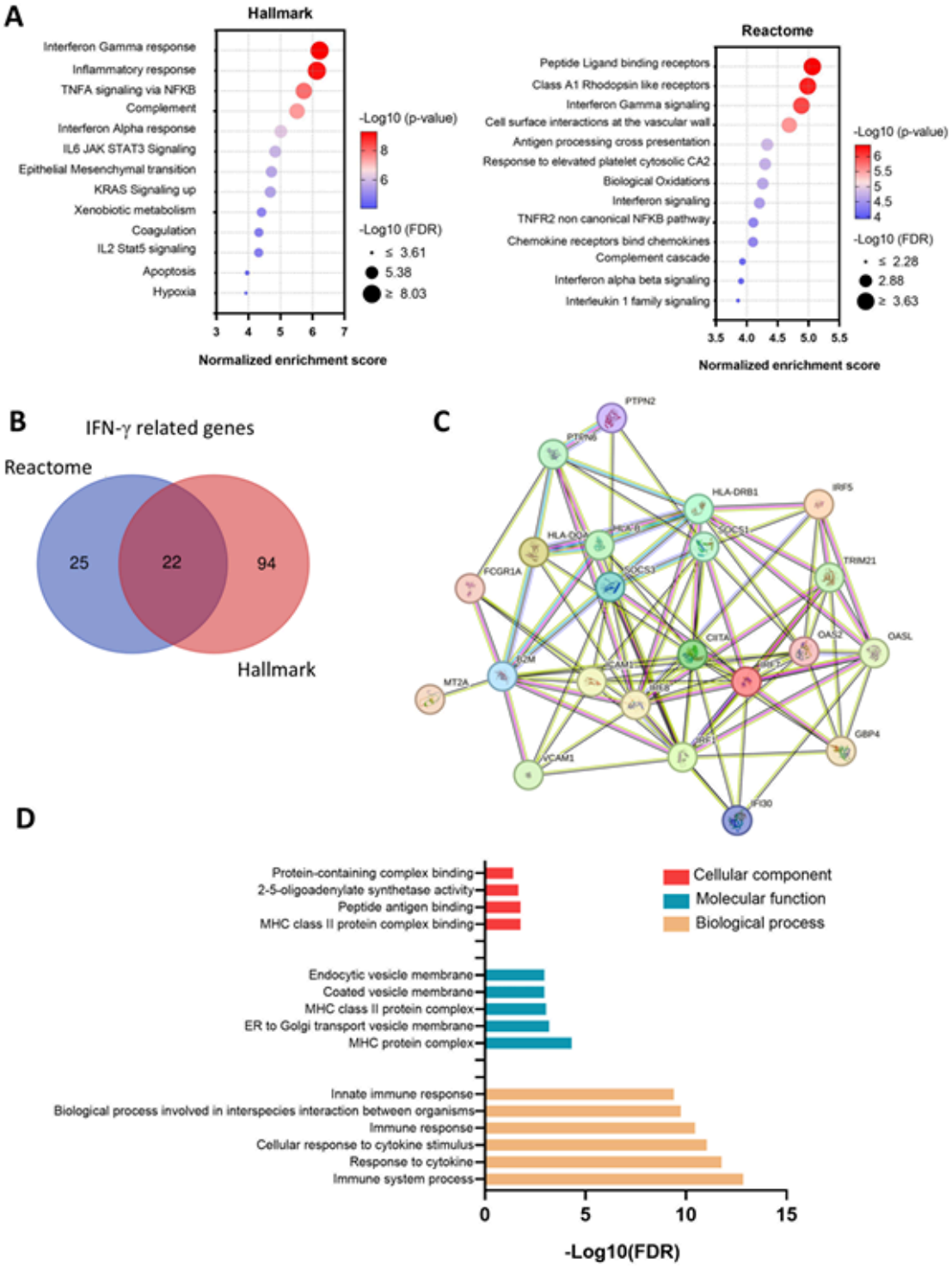
Table 1. Summary of metabolic-related pathways enriched in Membrane-Associated Protein 17 (*MAP17*).

Term	NES	*p*-value	FDR	Gene ID
Folate metabolism	3.6184	0.0003	0.0093	*SAA2*, *SAA1*, *CSF1*, *SERPINA3*, *SERPINE1*, *FOLR2*, *FOLR1*, *MTHFS*, *HBB*, *SOD2*, *SOD3*, *IL6*, *HBA1*, *CCL2*, *ICAM1*, *IL1B*
Zinc homeostasis	3.3921	0.0007	0.0183	*SLC39A12*, *MT1F*, *MT1E*, *MT3*, *MT1L*, *MT1X*, *MT1G*, *MT1H*, *SLC39A8*, *MT1M*, *SLC39A4*, *MT1A*, *MT2A*
Fatty acid metabolism	3.3367	0.0008	0.020	*ALOX15B*, *THEM4*, *ACADS*, *AMACR*, *ALOX5*, *GGT1*, *CBR1*, *ACADVL*, *MMAA*, *ACOX2*, *AKR1C3*, *PTGDS*, *DPEP2*, *ACOT13*, *CROT*, *ACADL*, *MID1IP1*, *CYP4F11*, *GGT5*, *GPX4*, *ALOX5AP*, *PTGES*, *PON3*, *CYP4F3*, *PON2*, *ELOVL7*, *GPX1*, *ACSF2*, *ACSL4*, *ACAA2*, *LTC4S*, *CYP2J2*, *HPGDS*, *ACSL5*, *ACSL6*, *MAPKAPK2*, *CYP1B1*, *TBXAS1*, *SLC22A5*, *ACOT11*, *PTGS2*, *ACBD4*, *PPT1*, *PTGR1*, *ABCC1*, *NUDT7*, *ACADM*, *ACOT4*, *ACSL1*, *PTGR2*, *HSD17B8*, *SLC25A20*, *PHYH*, *PTGS1*, *PECR*, *CYP2U1*, *ELOVL1*, *HSD17B12*, *HSD17B3*, *EPHX2*, *ECHS1*, *ACOT9*, *ABCD1*, *PRKAG2*, *ACACB*, *ALDH3A2*
Metabolism of vitamins and cofactors	3.041	0.0024	0.036	*BCO2*, *RETSAT*, *PPCS*, *APOE*, *VNN1*, *RBP4*, *NAMPT*, *APOC2*, *AKR1C3*, *ACP5*, *GPC4*, *LMBRD1*, *AKR1C1*, *SPR*, *RBP1*, *MOCOS*, *NNMT*, *PLB1*, *GCH1*, *LRP2*, *GCHFR*, *GPC5*, *TPK1*, *PARP8*, *SLC19A3*, *GSTO1*, *QPRT*, *PARP9*, *SLC25A19*, *ALDH1L1*, *SDC2*, *RNLS*, *VNN2*, *GSTO2*, *LRAT*, *NMNAT3*, *PTGS2*, *PARP14*, *PARP10*, *CD38*, *FOLR2*, *MTHFS*, *PNPO*, *BST1*, *SDC4*, *SLC2A3*, *PRSS3*, *AOX1*
Glycolysis gluconeogenesis	2.376	0.0175	0.111	*HK3*, *PCK2*, *PGAM2*, *ALDH9A1*, *ALDH7A1*, *ALDH2*, *GCK*, *ALDH3B1*, *GALM*, *ALDH3A1*, *ALDOA*, *HK2*, *ENO2*, *LDHA*, *FBP1*, *PGK1*

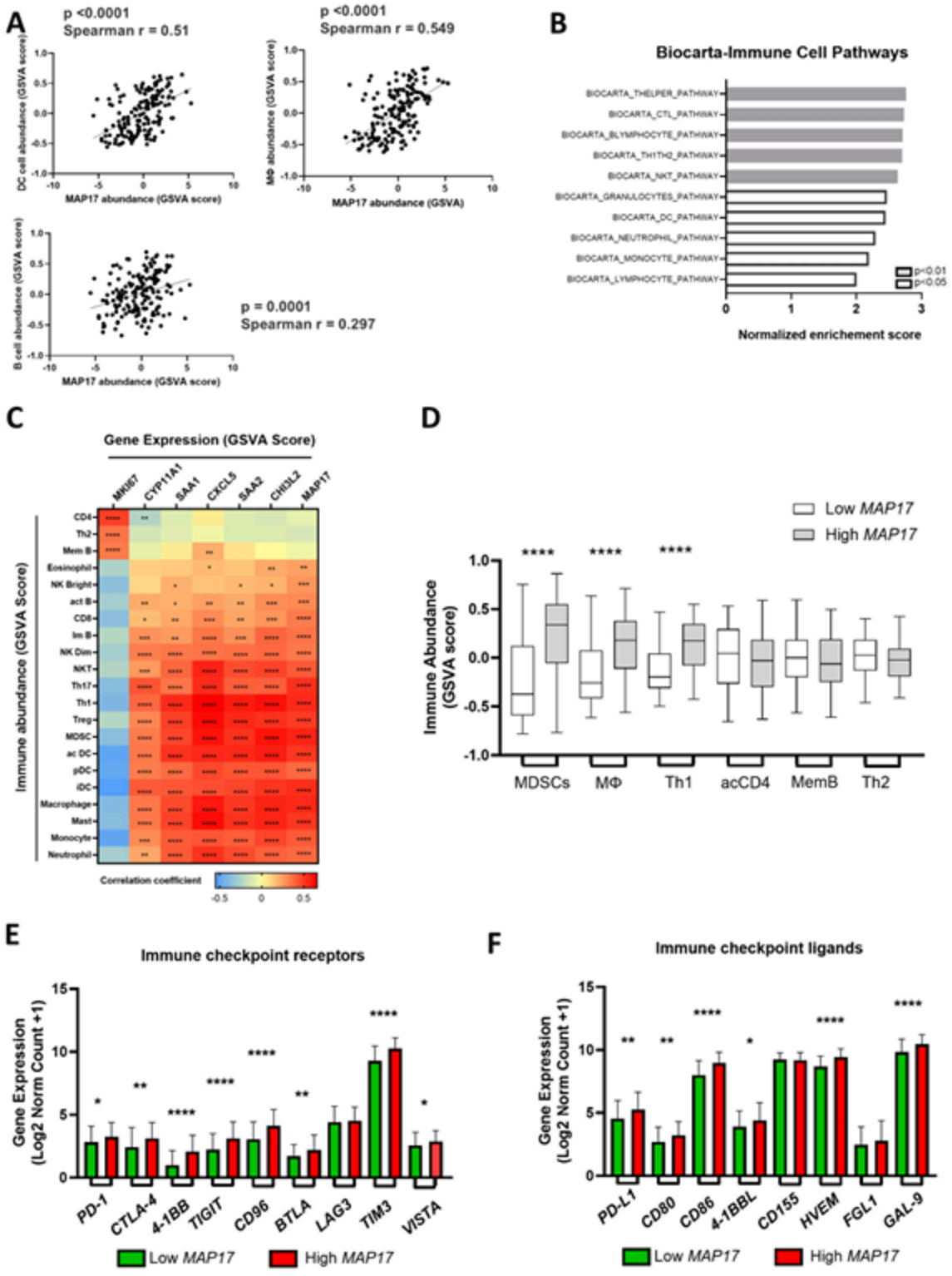
NES, Normalized Enrichment Score; FDR, false discovery rate; Gene ID, Gene Identification. The full names of the gene abbreviations are provided in **Supplementary**



High MAP17expression associated with cancer stem cells and metabolic processes.



MAP17 associated with IFN-γ-related genes and strong immune response.



The association between MAP17 and the immune microenvironment in GBM.

Methods and Results Summary

Here is a breakdown of the methods used and their corresponding results:

1. Data Sources and Analysis

- **Methods:**
  - Data from The Cancer Genome Atlas (TCGA)-GBM dataset was analyzed using bioinformatics tools such as UCSC Xena, GEPIA, TIMER 2.0, and TISIDB.
  - Gene expression and immune cell distribution were explored using RNA-sequencing data.
  - Differential gene expression (DEG) analysis and Gene Set Enrichment Analysis (GSEA) were performed to identify pathways enriched in MAP17-high vs. MAP17-low groups.
- **Results:**
  - MAP17 was identified as a key marker associated with the slow-cycling glioblastoma phenotype, characterized by quiescence, stemness, and therapy resistance.
  - Enrichment of mesenchymal and stem-cell-related pathways was observed in MAP17-high groups.
  - MAP17 was also associated with immune processes, such as immune checkpoint inhibitors and antigen presentation.

2. Survival Analysis

- **Methods:**
  - Kaplan-Meier survival analysis was conducted to compare overall survival (OS), disease-specific survival (DSS), and progression-free intervals (PFI) between high and low MAP17 groups.
- **Results:**
  - High MAP17 expression correlated with worse OS, DSS, and PFI, highlighting its prognostic value.

3. Immune Microenvironment and Pathway Analysis

- **Methods:**
  - Immune cell distribution was analyzed using TISIDB.
  - The STRING database was utilized for protein-protein interaction and pathway enrichment analysis.
  - Cytokine signaling pathways were explored using Hallmark and Reactome analyses.
- **Results:**
  - MAP17-high tumors showed an immunosuppressive microenvironment enriched in immune checkpoint inhibitors (e.g., PD-L1, TIM3, CTLA-4).

    - The tumors also exhibited pathways related to IFN-γ signaling, antigen presentation, and inflammation.

4. Histological Validation

- **Methods:**
    - Immunohistochemistry data from the Human Protein Atlas was used to visualize MAP17 expression in GBM tissues.
- **Results:**
    - High MAP17 expression was predominantly observed in mesenchymal glioblastoma subtypes.

5. Metabolic Pathways

- **Methods:**
    - Analysis of metabolic pathways enriched in MAP17-high groups, focusing on folate, zinc, and fatty acid metabolism.
    - Expression levels of transporters involved in these pathways were evaluated.
- **Results:**
    - MAP17 was strongly associated with metabolic pathways critical for the quiescent stem-like phenotype of glioblastoma cells.