

ABSTRACT NO:21
RESEARCH ARTICLE**Single-cell Transcriptomic Characterization of DPP8 and DPP9 Expression Across Malignant Transcriptional States in Glioblastoma**Malaika Khan ¹, Paras Jawaid ², Azhar Hussain ³, Syed Ather Enam ⁴**Abstract**

Objective: Glioblastoma (GBM) is a grade IV astrocytoma characterized by extensive intratumoral heterogeneity, with malignant cells existing in distinct malignant transcriptional states within the same tumour. DPP8 and DPP9 are intracellular serine proteases implicated in tumour progression and regulated cell death; however, their cell state-specific expression in GBM remains poorly understood. This study aimed to characterize the expression of DPP8 and DPP9 across malignant transcriptional states in GBM using single-cell RNA sequencing and to identify biological pathways associated with DPP8-high malignant cells

Methods: Single-cell RNA sequencing data (GSE131928) generated by Neftel et al. was retrieved from Gene Expression Omnibus (GEO). This study was conducted from June to August 2026. All analysis was performed in R (v4.6.1) using Seurat (v5.5.1). Following quality control and preprocessing, malignant cells were classified into four established transcriptional states (AC-like, MES-like, NPC-like, and OPC-like) using published meta-module gene signatures. DPP8 and DPP9 expression was evaluated across these cellular states. Differential expression analysis between DPP8-high and DPP8-low malignant cells, followed by Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment to identify the biological processes associated with DPP8-high malignant cells.

Results: Malignant cells were successfully classified into four transcriptional cellular states: astrocyte-like (AC), mesenchymal-like (MES), neural progenitor-like (NPC), and oligodendrocyte progenitor-like (OPC). DPP8 and DPP9 expression differed significantly across these cellular states. AC-like cells demonstrated the highest DPP8 expression followed by MES-like cells, while NPC-like and OPC-like cells exhibited comparatively lower expression. Cell-cycle analysis demonstrated significant differences across transcriptional states, with DPP8-high malignant cells showing enrichment of G2/M-associated signatures while largely comprising non-cycling cells. Differential expression identified distinct transcriptional programmes associated with DPP8-high cells. Functional enrichment analyses revealed significant enrichment of extracellular matrix organization, cell adhesion, and multiple signaling pathways.

Conclusion: Single-cell transcriptomic analysis demonstrates that DPP8 exhibits transcriptional state-specific expression of DPP8 in glioblastoma, with predominant expression in AC-like malignant cells. The identified molecular programmes provide biologically relevant hypotheses for the mechanisms underlying DPP8 function.

Key Words: Glioblastoma, Gene Expression Omnibus, Gene Ontology

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¹Centre Of Oncological Research in Surgery, Aga Khan University, Pakistan
Khyber Medical College, Pakistan, ²Centre Of Oncological Research in Surgery,
Aga Khan University, Pakistan, ³Centre for Regenerative Medicine and Stem
Cell Research, Aga Khan University, ⁴COORS (Center of Oncological Research in
Surgery) & Department of Surgery, Section of Neurosurgery, Aga Khan
University, Hospital, Karachi, Pakistan

Correspondence: Malaika Khan **Email:** malaikakhan1401@gmail.com

ORCID ID: 0009-0002-4588-7330