# Integration of RNA-Seq and proteomics data identifies glioblastoma multiforme surfaceome signature

## ABSTRACT

Background: Glioblastoma multiforme (GBM) is a highly lethal, stage IV brain tumour with a prevalence of approximately 2 per 10,000 people globally. The cell surface proteins or surfaceome serve as information gateway in many oncogenic signalling pathways and are important in modulating cancer phenotypes. Dysregulation in surfaceome expression and activity have been shown to promote tumorigenesis. The expression of GBM surfaceome is a case in point; OMICS screening in a cell-based system identified that this sub-proteome is largely perturbed in GBM. Additionally, since these cell surface proteins have 'direct' access to drugs, they are appealing targets for cancer therapy. However, a comprehensive GBM surfaceome landscape has not been fully defined yet. Thus, this study aimed to define GBM-associated surfaceome genes and identify key cell-surface genes that could potentially be developed as novel GBM biomarkers for therapeutic purposes. Methods: We integrated the RNA-Seq data from TCGA GBM (n = 166) and GTEx normal brain cortex (n = 408) databases to identify the significantly dysregulated surfaceome in GBM. This was followed by an integrative analysis that combines transcriptomics, proteomics and protein-protein interaction network data to prioritize the highconfidence GBM surfaceome signature. Results: Of the 2381 significantly dysregulated genes in GBM, 395 genes were classified as surfaceome. Via the integrative analysis, we identified 6 high-confidence GBM molecular signature, HLA-DRA, CD44, SLC1A5, EGFR, ITGB2, PTPRJ, which were significantly upregulated in GBM. The expression of these genes was validated in an independent transcriptomics database, which confirmed their upregulated expression in GBM. Importantly, high expression of CD44, PTPRJ and HLA-DRA is significantly associated with poor disease-free survival. Last, using the Drugbank database, we identified several clinically-approved drugs targeting the GBM molecular signature suggesting potential drug repurposing. Conclusions: In summary, we identified and highlighted the key GBM surface-enriched repertoires that could be biologically relevant in supporting GBM pathogenesis. These genes could be further interrogated experimentally in future studies that could lead to efficient diagnostic/prognostic markers or potential treatment options for GBM.