Single-cell characterization of human GBM reveals regional differences in tumor-infiltrating leukocyte activation

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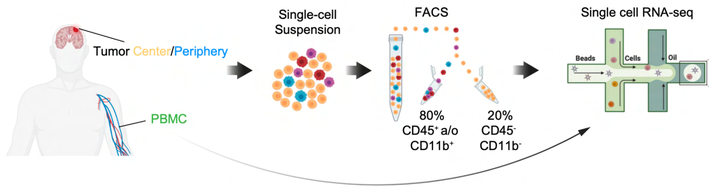
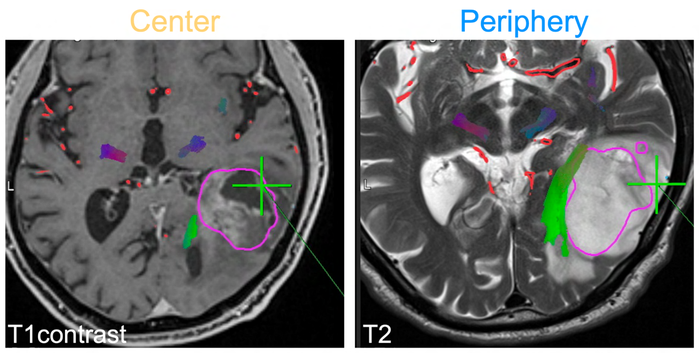
INTRODUCTION

Clinical trials of systemic T cell checkpoint blockade in GBM patients showed only disappointing results. This may be attributed in part to the immunosuppressive components of the GBM immune tumor microenvironment (iTME). Therefore, major efforts have been undertaken to describe the GBM iTME on a single cell level. However, human data on the composition of the iTME in different tumor regions (contrast enhancing tumor center versus peripheral infiltration zone) remain scarce.

METHODS



Here, we performed high-depth **single-cell RNA sequencing (scRNA-seq)** on **patient-matched** biopsies from **tumor center** and the **peripheral infiltration zone** of five primary GBM patients. Additionally, peripheral blood mononuclear cells **(PBMC) of the same patients** were included in the analysis to explore the transcriptional changes occurring during tumor infiltration of circulating immune cells. Main findings of the transcriptional analysis were confirmed by flow cytometry.

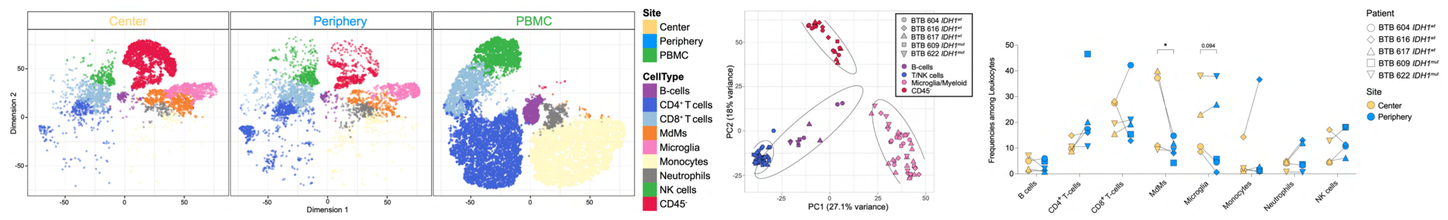


CONCLUSION

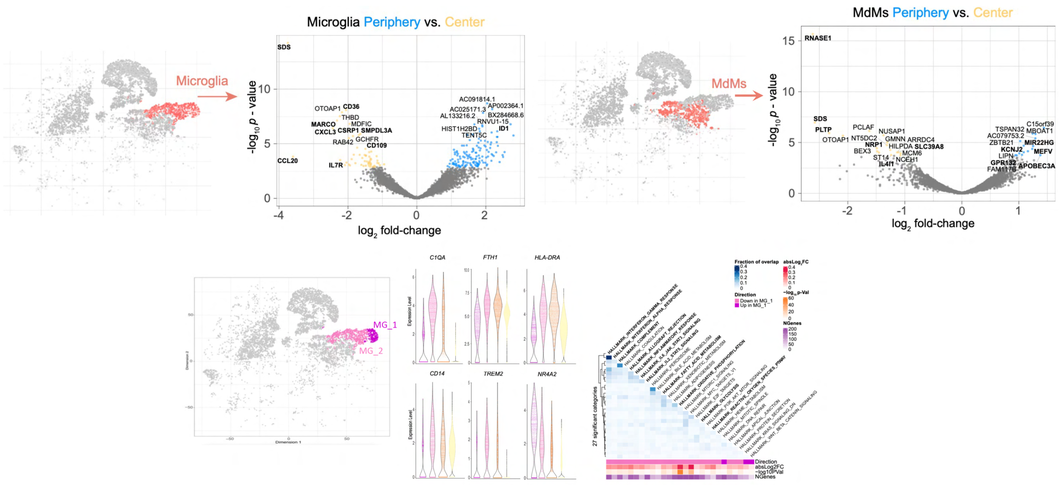
Our analysis provides a large-scale dissection of GBM-associated cell types complemented by patient-matched PBMCs, serving as a high dimensional reference map of the human GBM iTME.

RESULTS

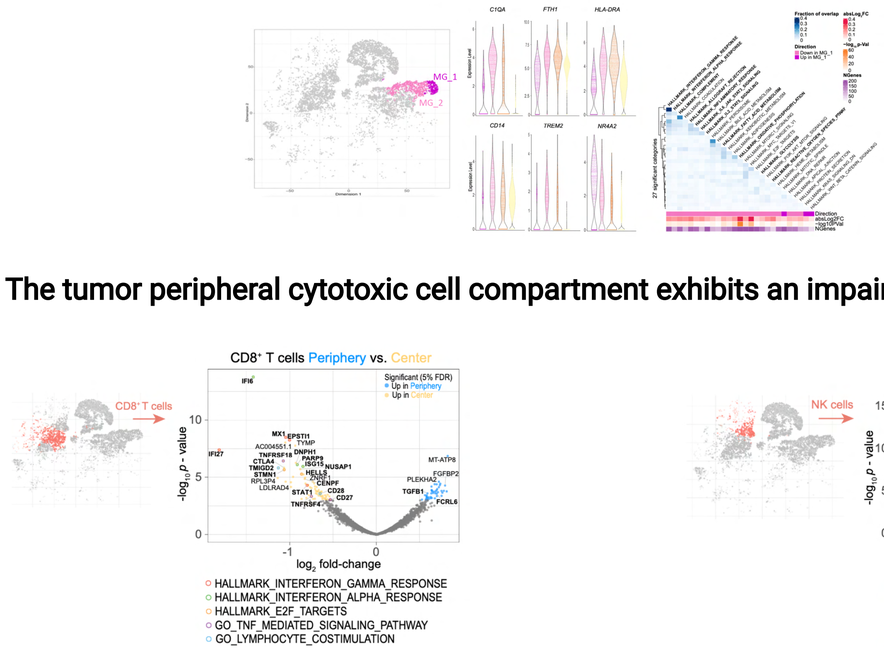
1. Single-cell RNA-seq analysis identifies main immune cell populations



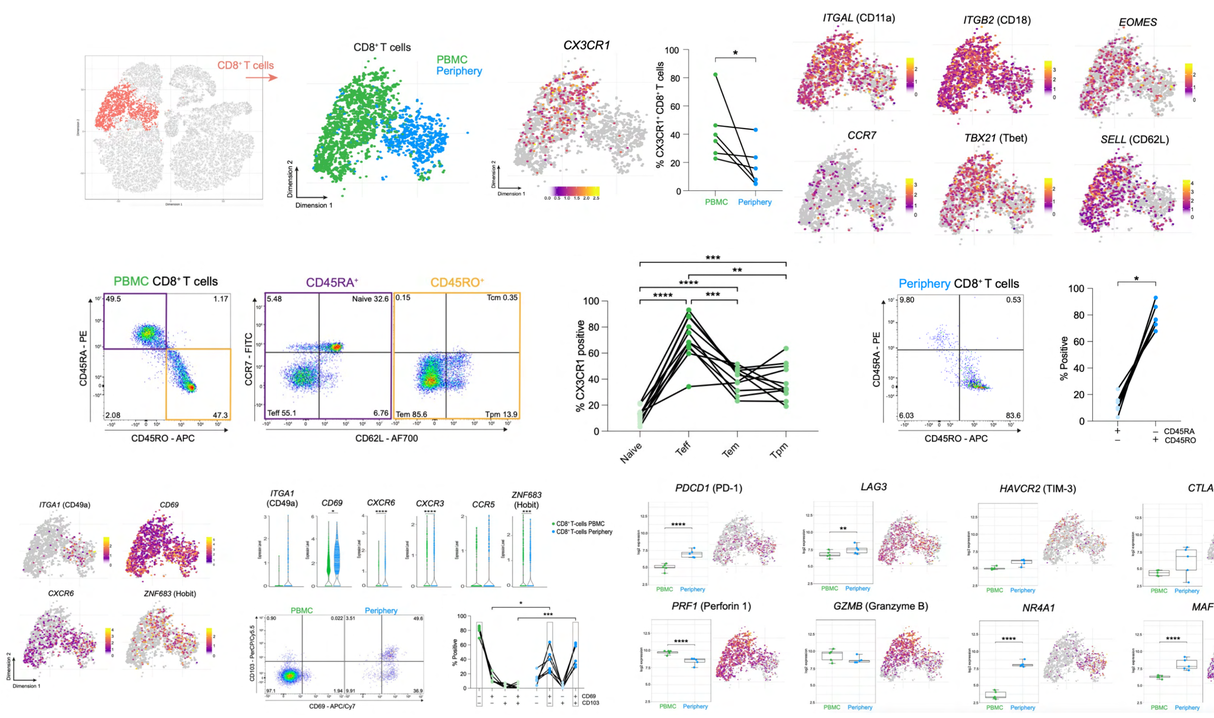
2. Microglia (MG) and monocyte-derived macrophages (MdMs) display distinct regional transcription profiles



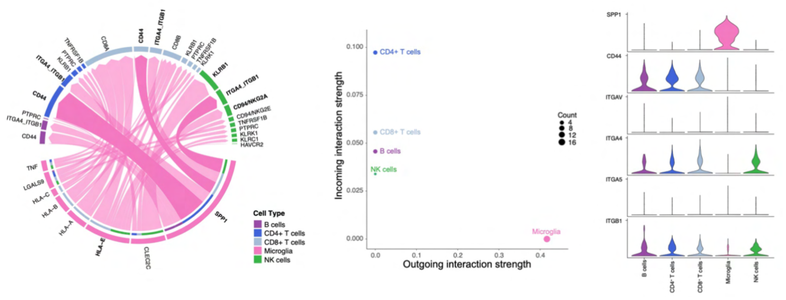
3. The tumor peripheral cytotoxic cell compartment exhibits an impaired activation signature



4. CD8+ T cells in grade 4 glioma show distinct memory phenotypes depending on site



5. Cell-cell communication analysis (CellChat) reveals critical role for SPP1-mediated crosstalk in tumor periphery



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