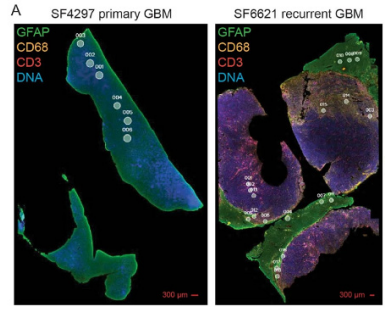
Digital spatial profiling enables creation of a glioblastoma cell atlas and reveals potential therapeutic targets

Background

- Glioblastomas (GBMs) have proven resistant to all genotoxic therapies employed in clinical trials
- Longitudinal studies have shown a lack of selection pressure for mutations under therapy
- GBM cells exhibit a high degree of phenotypic plasticity and transition between different cell states
- It is unknown how treatment by radiation, chemotherapy, resection, or immunotherapy influences this plasticity

Research Question

How does standard therapy of glioblastoma shape the milieu of tumor-associated immune cells and nonmalignant neuroglia?



Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Human Brain
Assay	Cancer Transcriptome Atlas and Immune Cell Profiling Core
Analyte	RNA and Protein
Readout	NGS and the nCounter® Analysis System

Why GeoMx?

An integrated analysis of spatial transcriptomics and snRNA-seq data was crucial to creating a single cell atlas of glioblastoma (GBM) and mapping paracrine signals in the GBM microenvironment and identifying therapeutic targets.

Geometric regions of interest (ROIs) were selected based on the presence or absence of immune cells and/or proximity to the tumor invasive margin. Figure reproduced with permission from Wang et al. Nat Cancer. 2022; 3(12) under the ***Creative Commons license.***

Results & Conclusions

- GBM patients undergo a PN (proneural) to MES (mesenchymal) shift at recurrence, concomitant with an increase in the birth rate of MES cells in recurrent tumors and supported by paracrine signals from the tumor microenvironment.
- Gene-expression correlates of the re-entry of previously quiescent MES cells into the cell cycle at recurrence were found and these genes decrease GBM cell viability.
- Hypermutation status was found to be a predictor of increased T-cell infiltration at recurrence, and increased T-cell infiltration at recurrence was prognostic.
- Spatial transcriptomics and proteomics validated the coexpression of intercellular paracrine and autocrine signals between neoplastic cells.
- CNTF, PTN or WNT3A could be likely therapeutic targets for GBM

Wang et al. Nat Cancer. 2022; 3(12) ***https://doi.org/10.1038/s43018-022-00475-x***

For more information, please visit nanostring.com/geomx

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MARCH 2023 MK5484