97 ULTRAHIGH-PLEX SPATIAL PHENOTYPING OF THE GLIOMA TUMOR LANDSCAPE IN IDH-1^{WT} AND IDH-1^{R132H} PATIENT TISSUES

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Background Glioblastoma (GBM) is the most common and aggressive malignant primary brain tumor in adults and is associated with poor prognoses despite aggressive treatments with surgical resection, chemotherapy, and radiotherapy. While immunotherapies have been approved for the treatment of various types of cancer, clinical trials in GBM treatment have yielded little to no success. The R132H mutation in the isocitrate dehydrogenase 1 gene (IDH-1^{R132H}) is the most important prognostic factor for the survival of glioma patients. IDH-1^{R132H} generates high levels of 2-hydroxyglutarate (2-HG) – an oncometabolite that modulates cellular epigenetic programs and metabolic profiles. Inactivating alpha-thalassemia retardation X-linked (ATRX) mutations frequently co-occur with IDH1 mutation, yet the mechanism(s) explaining their co-dependency, as well as their impact on the tumor microenvironment remain unknown.

Methods Using PhenoCode™, and epigenetics we performed a comprehensive analysis of over 70 proteins on the PhenoCycler®-Fusion spatial biology platform to study immune checkpoints, tissue structure, cellular activation states, and tumor landscapes in ATRX mutant gliomas with (n=2) and without (n=2) IDH-1 mutations.

Results Whole-slide single-cell spatial phenotyping analyses revealed high phenotypic diversity in the tumor immune microenvironment (TiME) of the GBM patients and added novel insights into the differential expression profiles of ATRX mutant, IDH-1^{WT} vs IDH-1^{R132H}. Via ultrahigh-plex single cell spatial phenotyping, we isolated spatial signatures within human FFPE GBMs and offer a deep analysis of the diverse cell types and functional states across the GBM IDH-1^{WT} and IDH-1^{R132H} tissues.

Conclusions In this study, we designed an antibody panel for a deep comparative analysis of the TiME and functional landscapes within the glioma tissues based on their IDH-1 status. Our data has enormous potential to deepen our understanding of the human GBM TiME and will help to develop new immunotherapies.

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