to enhance tumour growth and proliferation, particularly within the characteristic hypoxic tumour microenvironment (TME) of GBM. I hypothesize that the expression of ICAM1 on the surface of TAMs contributes to the presence of brain irradiation. Brain immune-profiling of brain irradiation-treated E0771-GFP-luc cells was indicated E2-depletion therapies could be used in combination with brain irradiation to decrease progression of BMs and promote an anti-tumour immune response.

CONCLUSIONS: It is evident that the hypoxic tumour microenvironment increases the expression of ICAM1 in macrophages. The tumour microenvironment increases migration levels of macrophages. The expression of ICAM1 in TAMs in hypoxic TME promotes GBM cell invasiveness, proliferation, aggressiveness and migration.

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INVESTIGATING CD8 T CELL EXHAUSTION STATES WITHIN THE TME AND DRAINING LYMPH NODE OF PRIMARY BRAIN TUMORS AND BRAIN METASTASES

Jessica Waibel Polanau, Alexandra Hoyt-Miggelbrink, William Tomaszewski, Peter Fecci; Duke University, Durham, NC, USA

Brain metastases affect nearly 20% of all cancer patients. Likewise, glioblastoma (GBM) is the most common primary brain cancer in adults and remains universally lethal. Current immunotherapeutic efficacy is hindered by immunosuppression present in the brain tumour microenvironment (TME). T-Cells, critical for tumor clearance, take on a functionally exhausted phenotype. Importantly, two exhaustion states, progresor (Tpe) and terminal (Tte), have been identified in models of chronic infection and cancer. This distinction is particularly relevant, as Tpe can remain responsive to immune checkpoint blockade (ICB), while Tte cannot. To date, the dynamics and characteristics of these exhausted populations in primary tumors and brain metastases remain unclear. Using intracranially implanted murine models of GBM (CT2A) and metastatic melanoma (B16F10), Tpe and Tte were identified by flow cytometry as PD1+SLAMF6+ and PD1+TIM3+, respectively. Functional differences between subsets were evaluated via intracanal staining of IFNg, TNFα, IL2, CD107a, and Ki67. To determine the role of antigen, we performed adoptive lymphocyte transfers of tumor-specific and non-tumor-specific transgenic T-cells into a TRP2 or OVA overexpressing intracranial CT2A or B16 tumor, respectively. Tpe displayed higher cytotoxic molecule expression than Tte, consistent with chronic infection models. Key exhaustion-associated transcription factors were identified in exhaustion subsets, including Tcf7, T-bet, and Eomes. AQP4 expression in particular or immortalized macrophages are treated with tumour cell-conditioned medium and is further exacerbated upon incubation of these cells in hypoxic conditions. The migration levels of bone marrow derived macrophage mouse cell type is higher in wild type cells than in ICAM1 deficient cells and higher when co-cultured with tumour cell condition media. ICAM1 deficient mice succumbed to GBM more quickly compared with wild type. CONCLUSIONS: It is evident that the hypoxic tumour microenvironment increases the expression of ICAM1 in macrophages. The tumour microenvironment increases migration levels of macrophages. The expression of ICAM1 in TAMs in hypoxic TME promotes GBM cell invasiveness, proliferation, aggressiveness and migration.