SINGLE CELL LANDSCAPE OF TUMOR INFILTRATING T CELLS IN ENDEMIC BURKITT LYMPHOMA PATIENTS

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The tumor microenvironment (TME) in endemic Burkitt lymphoma (eBL) contains not only malignant B cells infected with EBV but tumor infiltrating lymphocytes (TIL). Normal immune regulation involves checkpoints to limit immunopathology however, expression of inhibitory receptors and their cognate ligands within the TME can impede protective T cell function engaged in anti-tumor cytotoxicity. Using single cell RNA sequencing (scRNA-seq) we explored the heterogeneity in TIL subpopulations and immune inhibitory protein-ligand expression patterns within the TME from 6 Kenyan eBL patients. We found that $CD8^+$ TILs exhibited a linear progression from pre-dysfunctional state to a dysfunctional state expressing high levels of multiple inhibitory receptors such as TIGIT, LAG3 and TIM3. Using unbiased analyses, a total of five clusters emerged, each with a unique gene expression signature. Three of these clusters expressed high levels of multiple exhaustion markers such as TIGIT, TOX, CTLA4, and CXCL13, and were classified as $CD8^+$ exhausted T cell (Tex) populations. Immunohistochemical staining of 15 BL FFPE tumor sections validated the expression of PD1 and TIGIT on CD8+ T cells and PD-L1, PVR, and Nectin-2 on BL tumors which were scored based on their expression levels. We were also able to detect viral protein expression for BZLF1 demonstrating foci of lytic reactivation within the TME. These pre-clinical findings provide a strong rationale for risk-stratifying patients who might benefit from immune checkpoint inhibitor therapy to improve patient outcomes.

The most appropriate topic area "EBV and tumor microenvironment".

Oral presentation preferred.

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