AB154. 193. The effect of the tumour microenvironment on T-cell differentiation and effector subsets

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Background: Tumour infiltrating lymphocytes (TIL's) are capable of mounting an anti-tumour response. TIL's, however encounter a myriad of suppressive elements in the tumour microenvironment (TME), such as regulatory immune cells, soluble factors released by tumour cells and the presence of inhibitory molecules on the surface of tumour cells. Metabolic competition within the TME results in the modulation of immunometabolism, which may skew the T-cell response to a pro-tumour like phenotype resulting in exhaustion and failure to carry out effector functions. Understanding the impact of elements within the TME is vital to improving responses to new therapies such as immunotherapy. We aim to evaluate the impact of nutrient deprivation and hypoxia, common elements of the TME on T-cell differentiation and effector subsets.

Methods: A human CD4+ T-cell line (Jurkat) was cultured in media simulating aspects of the TME. Nutrient deprivation was simulated using glucose and glutamine free media, Severe hypoxia (0.5% O_2) was induced using the Don Whitley Hypoxystation. T cells were analysed by Flow Cytometry and effector subset differentiation was evaluated by transcription factors expression (T-bet, EOMES, FOXP3, GATA3, RORyt).

Results: T-cells cultured in conditions of hypoxia and nutrient deprivation had altered expression of transcription factors suggesting that nutrient deprivation within the TME can affect TIL subsets and potentially plasticity.

Conclusions: This study demonstrates that metabolic competition within the TME polarises T-cell responses by directly guiding the differentiation of distinct effector subtypes. Therefore, targeting T cell metabolism represents a promising immunomodulatory therapy for use in combination with immunotherapy

Keywords: Immunometabolism; tumour infiltrating lymphocytes (TIL's); T-cells; tumour microenvironment

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