Characterisation of the tumour immune microenvironment in bladder cancer: Implications for Predicting and Improving Therapeutic Response

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The tumour immune microenvironment (TIME) in solid tumours can be categorised into distinct states, including an "immune hot environment", which is characterised by high T cell infiltration; an "immune desert environment", which has few/no infiltrating T cells; an "inflamed, infiltrated but suppressive environment"; and an "immune cell excluded" environment.

To date, the TIME in bladder cancer has primarily been studied using transcriptomic deconvolution or single-cell RNA sequencing. However, spatially resolved analyses are currently lacking.

In this study, we are performing imaging mass cytometry using the Human Immuno-Oncology Panel and the Human Immune Cell Expansion Panel (Fluidigm) on 60 samples from 35 patients with bladder cancer.

Here, we present initial results from three patients. A195B displayed high infiltration of $CD8^+$/$PD\text{-}1^+$ T cells in tumour and stromal areas, whereas X055B and X057B harboured lower numbers of $CD8^+$ T cells. A high proportion of $CD68^+$ and $CD206^+$ macrophages were found in samples A195B and X057B and were specifically localised at the tumour/stroma interface in A195B. In these areas, PD-L1 was also detected.

To associate TIME features with therapy, we measured activation-induced markers on T cells following treatment with nivolumab in patient-derived fragment cultures. Despite the presence of $CD8^+$/$PD\text{-}1^+$ cells, we did not observe activation of $CD8^+$ T cells in A195B, indicating that these alone do not always predict functional immune responses. This highlights the importance of considering their spatial localisation and presence of immunomodulatory cell subsets.

Together, our initial results highlight the potential of combining IMC with preclinical testing of therapeutic responses to define how the TIME is associated with clinically relevant responses to therapy.