

Immune Profiling of the Tumour Microenvironment in Prostate Cancer Using Multiplex Immunofluorescence

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Purpose of the study: Prostate cancer (PCa) is known for its biological and clinical heterogeneity and identifying patients with an aggressive course is critical for providing radical interventions. Molecular profiling using immune cell phenotyping markers is vital to understanding the interactions of tumour infiltrating immune cells with malignant prostate epithelium. The aim of this study was to investigate the in situ phenotype, functional status and localisation of infiltrating immune cells in patients with PCa in order to determine whether they correlate with the ability of a tumour to metastasise to regional lymph nodes. We used a multiplex immunofluorescence (mIF), machine learning and automated quantitative scoring approach.

Methodology: A matched TMA was created from 94 patients who underwent radical prostatectomy with and without regional lymph node involvement. Two multiplex fluorescence panels for CD4, CD8, FoxP3, PD1 and CK and CD68, CD163, CD20 and CK were optimised and used for staining. We quantified the densities of those markers within the tumour epithelial and stromal compartments.

Results: Patients without lymph node metastasis had significantly more epithelial and stromal M1-like macrophages ($p=0.046$) and CD8 cytotoxic cells ($p=0.001$, $p=0.008$). They were also richer in stromal effector CD4 cells ($p=0.0003$). The stromal CD4 effector immune cell density was a significant predictor of lymph node spread in the univariate and multivariate analysis. An independent TMA of 184 patients was also stained with the same mIF panels and the stromal CD4 effector cell density remained a significant independent predictor of nodal spread.

Conclusion: Together, these findings suggest differences in the immune infiltrate (particularly CD4 effector T cells) between PCa patients with vs without lymph node metastasis. This is important because it suggests further investigation is necessary into how immune microenvironment can affect clinical outcome.