

MYELOID AND T CELL SUBSETS DEFINED IN BLADDER CANCER USING SINGLE-CELL RNA SEQUENCING AND PAIRED PROTEIN PROFILING<http://dx.doi.org/10.1136/jitc-2022-SITC2022.1054>

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Background Muscle-invasive bladder cancer (MIBC) has a 5-year survival of only 50% despite preoperative chemotherapy and radical cystectomy. For non-muscle-invasive bladder cancer (NMIBC), the 5-year survival rate is > 80%, but the local recurrence rate is very high. Immune checkpoint inhibitors can drastically increase survival, however only a fraction of bladder cancer patients is currently responding. We have performed single-cell RNA sequencing (scRNAseq) of tumor-infiltrating immune cells from NMIBC and MIBC biopsies as well as full-length scRNAseq with parallel protein profiling of T cells in MIBC, to pinpoint novel targets for immunomodulatory therapy.

Methods Tumor biopsies obtained from untreated patients with MIBC (N= 14) and NMIBC (N=4) were mechanically and enzymatically digested into single cell suspensions and either CD45⁺ or CD3⁺ cells were sorted. Parallel protein assessment (index sorting) was performed for CD3⁺ cells. In total, 30 000 CD45⁺ and 4061 CD3⁺ cells were processed according to the 10x Genomics and Smart-seq3 protocols, respectively.

Results Approximately 1600 and 4000 genes per cell were detected using the 10x and Smart-seq3 methodologies, respectively. The transcriptomic immune cell landscape in NMIBC and MIBC was delineated and within the myeloid compartment, e.g. SPP1⁺ tumor associated macrophages (TAMs) were identified and shown to correlate with response to checkpoint blockade in the IMvigor210 cohort.¹ Within the T-cell compartment, populations including cytotoxic CD4⁺ and CD8⁺ T cells and exhausted CD8⁺ T cells were identified and their transcriptional profiles were defined. Of note, using protein-level data from the index sorting, two populations of cytotoxic CD4⁺ T cells with remarkable similarity to CD8⁺ counterparts were identified. Furthermore, CD56⁺ T cells were found to differentially populate certain T cell clusters, including Treg and cytotoxic T cell clusters.

Conclusions Our results provide new insights into the myeloid and lymphocyte compartment in the microenvironment of bladder cancer. This understanding can give clues for designing novel treatment strategies.

REFERENCE

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Ethics Approval The study was approved by the Research Ethics Board of Lund University (Dnr 2017/269 and 2018/963) and Stockholm University (Dnr 2020-05559). Written informed consent was obtained from the patients for publication of the results.

Consent Written informed consent was obtained from the patient for publication of this abstract and any accompanying images. A copy of the written consent is available for review by the Editor of this journal.