

Direct Imaging Characteristics of Myeloid Derived Suppressor Cell (MDSC) Populations in Renal Cell Carcinoma Patients (RCC) by Ethnicity – An Exploratory Analysis

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Conclusions

RCC tumor samples appear to be primarily infiltrated by Granulocytic MDSC, ethnicity may potentially influence the spatial distribution of MDSC and should be investigated in further studies.

Introduction : MDSC are a key mediator of resistance to immune checkpoint blockade. Previous studies in RCC have investigated peripheral MDSC via flowcytometry. Multiplexed immunohistochemistry (mIHC) now allows direct visualization of MDSC in tissue, thus enabling spatial analysis of these populations. We hypothesized ethnic differences may influence spatial patterns of MDSC

Methods:

RCC samples (n=10) were obtained from the UAB tissue biorepository, with 5 Caucasian and 5 African American samples each. Paraffin sections were stained by the Ultimapper I/O MDSC 5 Plex kit for CD11b, CD14, CD15, HLA-DR, and a nuclear counterstain. Granulocytic (PMN)-MDSC were defined as being [CD11b+, CD15+, HLADR-Low], and monocytic(M)-MDSC were identified as [CD11b+,CD14+,HLA-DR-Low]. Digitally imaged slides were marked for tumor versus non tumor areas. An Image analysis algorithm (QuPath) was trained by a qualified pathologist to identify specific MDSC Cell populations based on mIHC expression. Once trained, the algorithm generated gaussian heat maps to compare areas of high and low MDSC distribution. These populations were compared in tumor vs non-tumor areas between patients of different ethnicities.

Results: PMN-MDSC were the most predominant population of tumor infiltrating MDSC (74%). MDSC comprised 0.56% (95%CI 0.1%-0.9%) of tumor cells, and 0.31%(95%CI 0.1-0.11%) of stromal cells and did not differ by race (p=0.85). When comparing the proportions of tumor infiltrating MDSC with total MDSC, trends were noted in Caucasian versus African American tumor samples [(5% vs 33%), p=0.07], in addition to differences in the Ratios of MDSC populations in tumor vs stroma [Caucasian (47%)vs African American (196%), p=0.08]

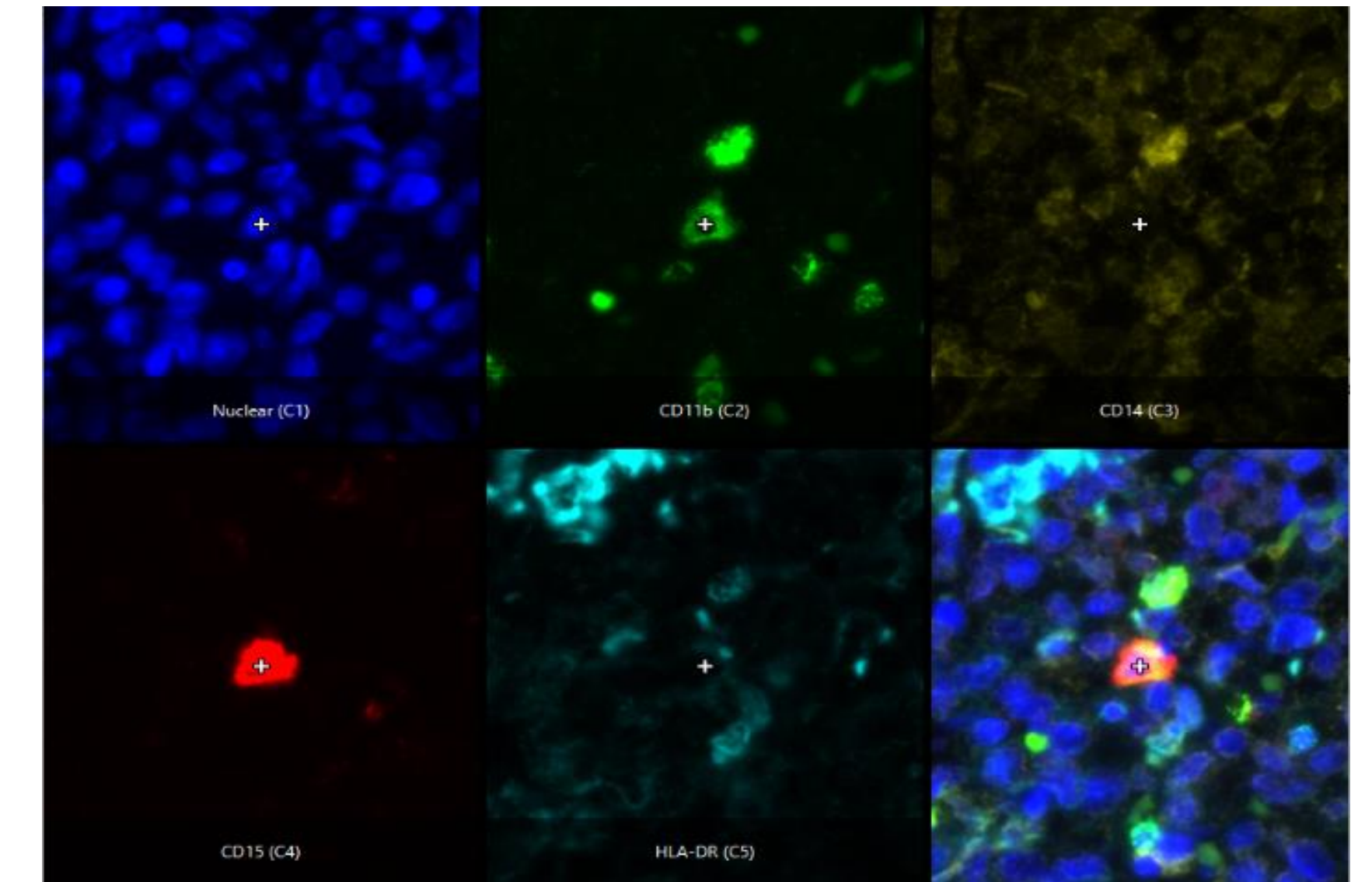


Fig 1: Characteristic immunostaining of a polymorphonuclear myeloid-derived suppressor cell (PMN-MDSC) [CD11b+ (green), CD14- (yellow), CD15+ (red), HLA-DR/low (cyan)] as identified in multichannel view of RCC tissue stained with multiplex immunofluorescence

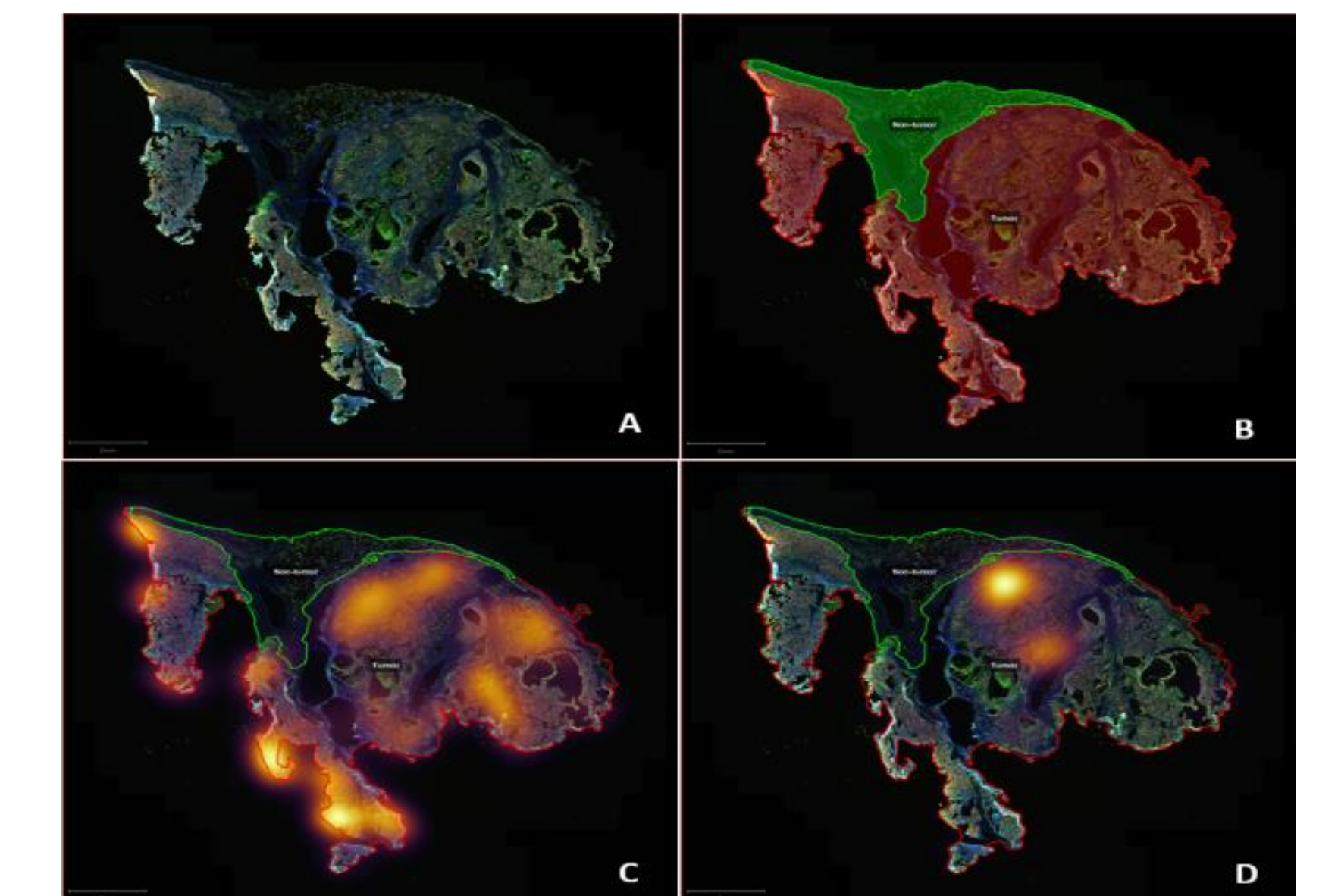


Fig 2:A. digital whole slide image. B] tumor (red in B) and non-tumor (green in B) areas noted by pathologist +QuPath. Density heatmaps for PMN-MDSC (C) and M-MDSC (D)

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