Identification of two functionally distinct subsets of macrophages infiltrating human breast cancer

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Introduction and Objectives: Tumor associated macrophages (TAMs) infiltration is a hallmark of solid tumors and generally correlates with poor prognosis. However, TAMs cellular diversity remains ill-defined in human tumors. Here we perform an unbiased single cell RNA sequencing approach on breast cancer metastatic lymph nodes (LNs) and primary tumor to characterize TAMs diversity. Methods and Results: We identify two major populations of tumor-associated CD14+ cells: S100A8+CCR2+APOE- monocytes and S100A8-CCR2-APOE+ macrophages. Using flow cytometry analysis and immunochemistry, we show that: 1) APOE+ macrophages are enriched at the tumor border within metastatic LNs, 2) S100A8+CCR2+ monocytes are associated to non-metastatic LNs and healthy breast tissues. APOE+ macrophages can be further subdivided in two populations: 1) APOE+TREM2+ TAMs expressing SPP1, CADM1 and FN1 and 2) APOE+FOLR2+ TAMs expressing SEPP1, MMP9 and SLC40A1. The transcriptional signature of APOE+TREM2+ TAMs negatively correlates with patient survival. By contrast, the transcriptional signature of APOE+FOLR2+ TAMs is a predictor of survival. Conclusion: This suggest that the two TAM populations may have opposite effect on tumor progression. Collectively, our data reveal the diversity of CD14+ cells and TAMs within breast cancer tumors and provide the molecular basis to assess their unique functional properties.

Keywords : Tumor-Associated Macrophages, Single cell RNA-seq, Breast Cancer, Tumor-draining lymph nodes
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