Immune Infiltrate Profiling of Cutaneous Melanoma with Spatial Transcriptomics

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Background and Objective:

In 2023, an estimated 97,610 melanomas will be diagnosed in the U.S. Immunotherapy has revolutionized care for melanoma patients and highlighted the prognostic value of characterizing immune infiltrates in melanoma tissue. This project used spatial transcriptomics (ST) to analyze immune infiltrates in cutaneous melanoma specimens.

Methods:

Visium Spatial Gene Expression platform generated datasets from formalin fixed paraffin embedded cutaneous melanoma specimens were analyzed using Loupe Browser software v6.5.0 (10x Genomics Inc.). Unsupervised clustering and manual region selection identified areas enriched in immune cell specific differentially expressed genes (DEGs). The transcript for Collagen alpha-1(XIX) chain (*COL19A1*) was identified as a DEG co-expressed with B cell marker DEGs. Fluorescence activated cell sorting was used to isolate primary B and T cells from mouse secondary lymphoid organs and human peripheral blood mononuclear cells to measure *COL19A1* with quantitative PCR (qPCR).

Results:

Transcripts for *CD19* (B cell marker) were concentrated in an immune DEG- rich region adjacent to a melanoma micrometastasis in one specimen. There was overlap between the tertiary lymphoid structure [TLS] markers *SELL*, *CXCR5, CCR7,* and *CXCL13* with *CD19* and/or *COL19A1*. Though qPCR revealed minimal *Col19a1* in mouse B and T cells, *COL19A1* was abundant and specific for human B cells.

Conclusions & Potential Impact:

This study demonstrates the feasibility and potential of using ST to characterize immune cell infiltrates in melanoma. Though *COL19A1* expression is typically understood to be enriched in muscle and neuronal cells, the studies presented here suggest this transcript could be a novel human (but not mouse) B cell marker. Future studies are needed to determine if collagen XIX (protein) is expressed in B cells and if it is, what the biological functions of this protein are in B cells under physiologic and pathologic (e.g. melanoma) conditions.