Spatial Transcriptomic Profiling of Cutaneous Melanoma Progression

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Background and Objective:
In 2022, an estimated 99,780 new melanomas will be diagnosed in the United States. As incidence rates continue to rise, identification of biomarkers for disease progression is urgently needed to prevent overdiagnosis and provide therapeutic targets. The purpose of this project was to determine if spatial transcriptomics can be used to identify transcript changes during melanoma progression.

Methods:
For this study and after specimen quality control (via DV200 values), four archival formalin fixed paraffin embedded (FFPE) human melanoma specimens were processed using the Visium Spatial Gene Expression platform. In Loupe Browser v6.0.0. (10x Genomics Inc.), K-means clustering was used as an unbiased approach in addition to manual selection of areas of melanoma adjacent to and distant from (i.e. nonadjacent) the epidermis to determine regions of interest for identification of differentially expressed genes (DEGs)

Results:
Expression of *PAEP* was significantly increased in a micrometastasis (~7.2 fold; Log_2 scale) versus the primary melanoma in one specimen. Other DEGs also distinguished the micrometastasis (*SLC16A3*, *CCND1*, *SCML4*, and *CSAG3*) from this primary melanoma (*S100A14*, *TRIM29*, *PTPRZ1*, and *BCAN*). In the other specimens, a similar pattern of differential gene expression was seen between areas of melanoma adjacent to and nonadjacent to the epidermis. In addition, K-means clustering identified a region of differential gene expression suggestive of an inflammatory cell infiltrate next to the *PAEP*-enriched micrometastasis.

Conclusions and Potential Impact:
This study demonstrates the feasibility of using spatial transcriptomics to investigate transcriptional changes during melanoma progression. Increased *PAEP* transcripts and the immunosuppressive functions of PAEP suggest PAEP may be an important mediator of melanoma progression. The current study suggests increased *PAEP* transcript levels are associated with inflammatory cell infiltrates. Understanding mechanistic links between increased *PAEP* and inflammation during melanoma progression could provide prognostic and therapeutic insights and thus, improved care for melanoma patients.