Spatial transcriptomics of TNBCs show an association between HOXB13 expression and formation of a plasmablast-rich neighborhood

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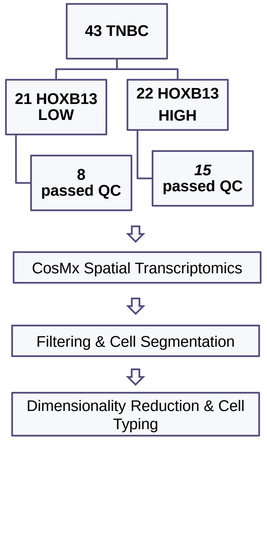
Introduction

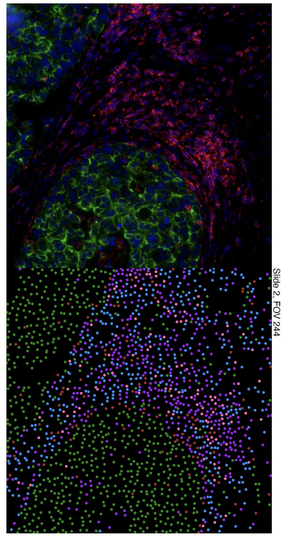
***HOXB13* Biomarker:** HOXB13 gene expression in combination with IL17RB has been extensively studied in hormone receptor positive (HR+, HER-) post-menopausal breast cancer patients as a marker of treatment response to extended adjuvant endocrine therapy. Recently, we demonstrated that HOXB13 is expressed in a subset of triple negative breast cancer (TNBC) patients.

Immune-Connection: Immunotherapies are now being evaluated for use in TNBC. Ectopic expression of HOXB13 in a mouse mammary model of TNBC confers a tumoral growth advantage by impeding antitumor T-cell immunity. Here, we performed comparative spatial transcriptomic profiling of the immune microenvironment of HOXB13+ and HOXB13- human TNBCs.

Study Goal: Despite the independent development and validation of the *HOXB13/IL17RB* gene expression ratio as a prognostic and predictive biomarker, the specific molecular underpinning of these two genes remains unknown. In this study, we sought to determine whether human tumors might recapitulate the results observed in mouse models and further probe their molecular mechanisms.

Methods





Results

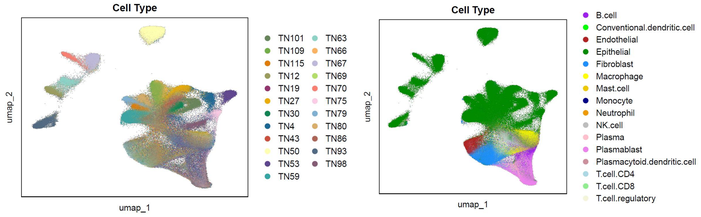


Figure 1: Cells were segmented based on gene expression data and cell type or specimen source overlayed to look for potential artifactual differences.

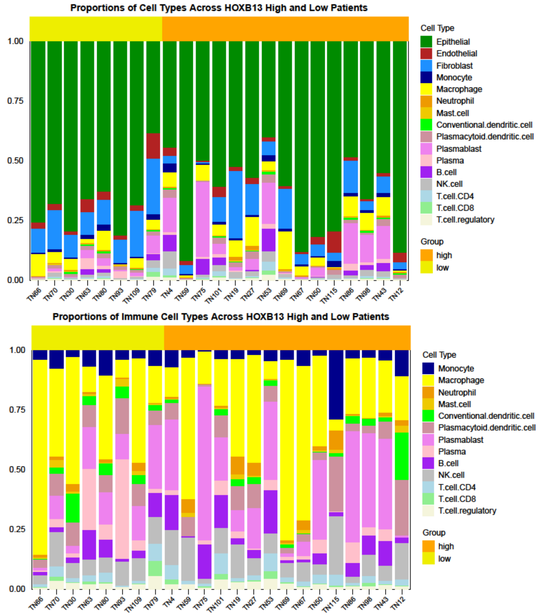


Figure 2: A relative breakdown of cell types were plotted per patient and per HOXB13 status to look for relative differences across patients.

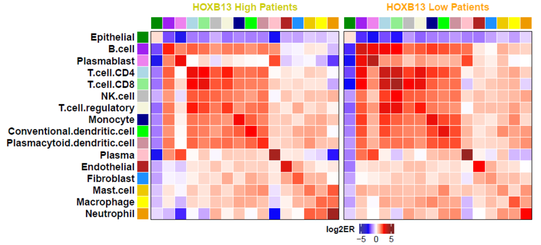


Figure 3: Analytical neighborhood enrichment analysis for each cell type was conducted using a spatial neighborhood graph constructed by Delaunay triangulation.

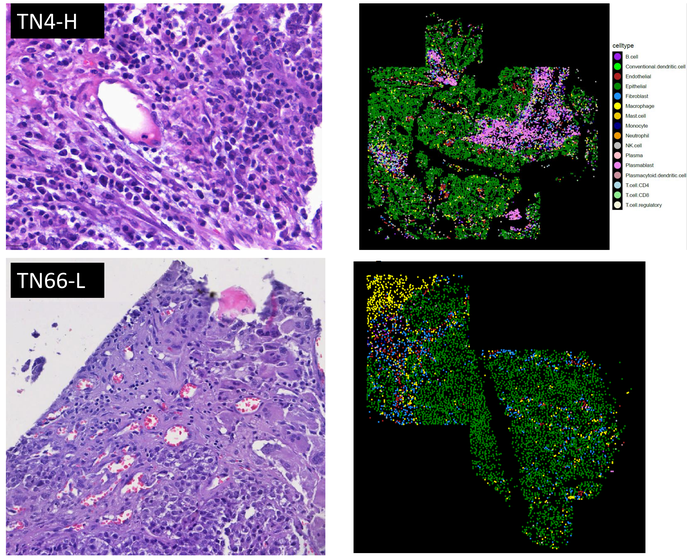


Figure 4: Histological images were reviewed to confirm the presence of abundant plasma cells in the designated cases. These results were further correlated with the cell segmentation spatial maps.

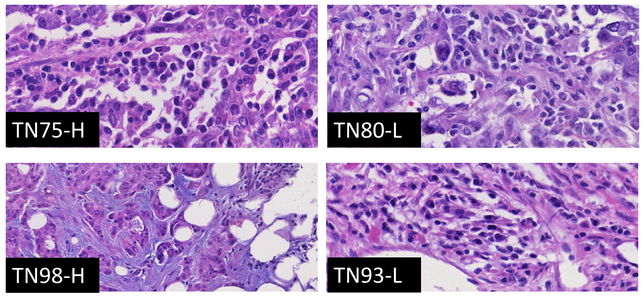


Figure 4 continued with additional HOXB13 high (H) or low (L) images.

Conclusions

- Spatial transcriptomics analysis of breast tissue can accurately map the distribution of immune cells in the tumor microenvironment.
- A plasmablast-rich immune neighborhood is more frequently seen in HOXB13+ rather than HOXB13- TNBCs, and such a neighborhood is not associated with CD8+ T cells.
- We have recently shown that HOXB13 expression in a preclinical model impedes anti-tumor immunity. Our findings raise the possibility that plasmablasts may directly suppress CD8+ T cells or that the formation of these plasmablast-rich neighborhoods occupies a niche that comes at the cost of anti-tumor/cytotoxic neighborhoods.

Funding

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