Identifying Differences in Spatial Transcriptomics Between Subtypes of Pancreatic Ductal Adenocarcinoma

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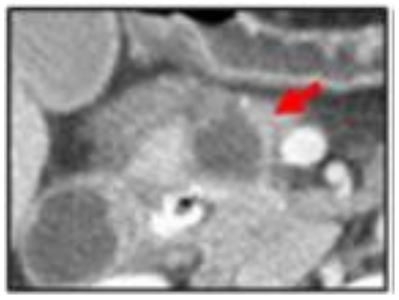
Introduction

Pancreatic ductal adenocarcinoma (PDAC) is an aggressive and lethal form of pancreatic cancer, ranking fourth in cancer-related deaths in the US. PDAC is heterogenous in its biophysical features and clinical outcomes.[1] Characterization of tumors into distinct biological subtypes would enable more personalized therapies. The “delta” method is used to characterize the interface between the border of tumor and healthy pancreas on CT scans before treatment. High delta tumors are more conspicuous on CT scans, and patients with these high delta phenotypes have earlier distant metastasis, and shorter overall survival than patients with tumors classified as low delta, which are less conspicuous on CT.[2]

A.



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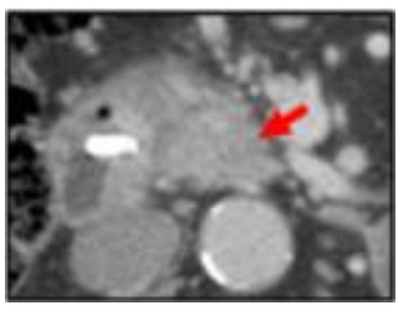


Figure 1. Arrows pointing to highly conspicuous tumor, or high delta (A) and less conspicuous PDAC tumor, or low delta (B) on CT.[2]

Through molecular characterization, two PDAC subtypes are known: classical, which are frequently surgically resectable, and basal-like, with poorer clinical outcome.[3]

There is a gap in knowledge regarding the transcriptomic differences between high and low delta tumors. Here we aim to investigate the spatial transcriptomic (ST) differences between high and low delta tumors. By using ST, we will measure gene activity and map where the gene clusters are on the tissue.

Materials and Methods

Using 20 tumor samples, ten classified as high delta and ten as low delta, we first consulted with a pathologist to identify tissue regions of high cancer density. Using these regions, we will continue gathering data with the 10X Genomics ST protocol.

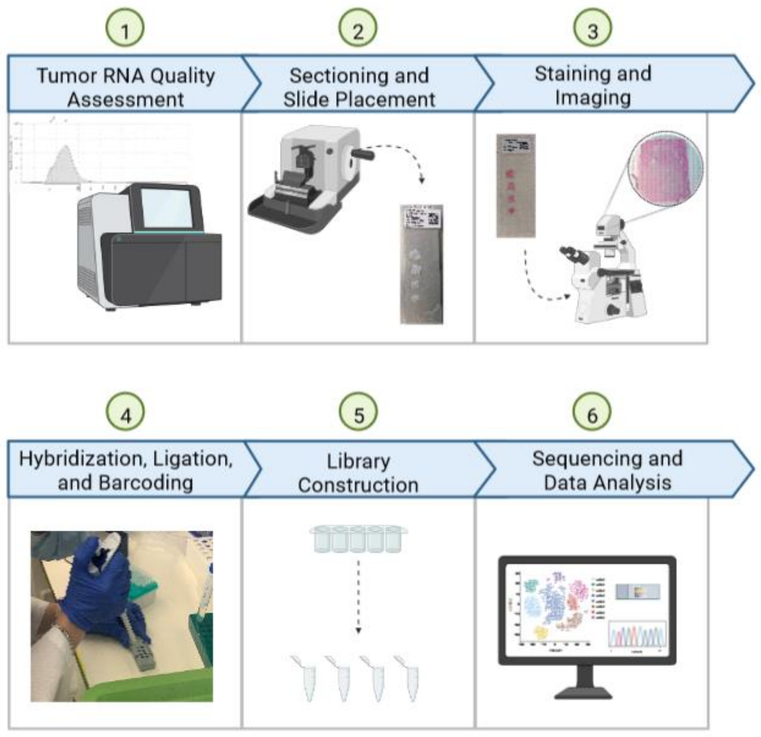


Figure 2. Pathway displaying how tumor tissues were evaluated and prepared to obtain sequencing and spatial expression information.

Results

Currently, four samples are awaiting to be sequenced and 16 are in the process of hybridization, ligation and barcoding. Two preliminary FFPE tissue samples were analyzed to compare low and high delta tumors.

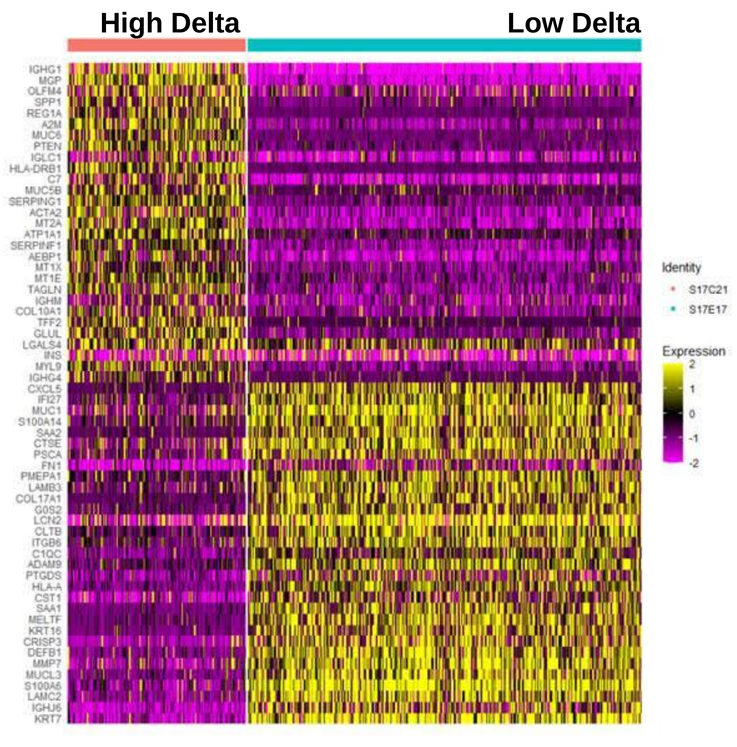
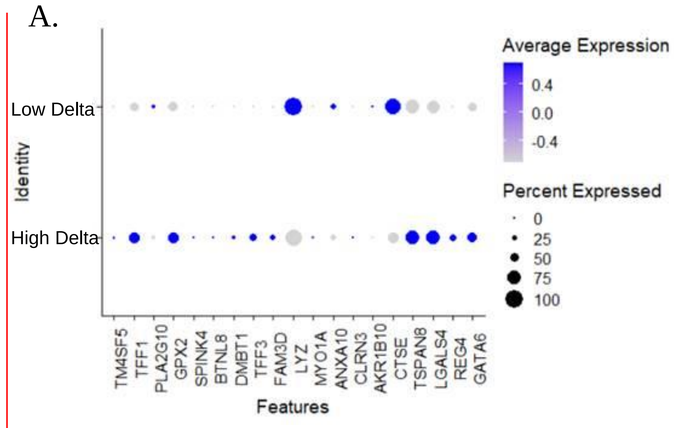


Figure 3. Comparison of transcriptional profiles between high and low delta tumors.

A.



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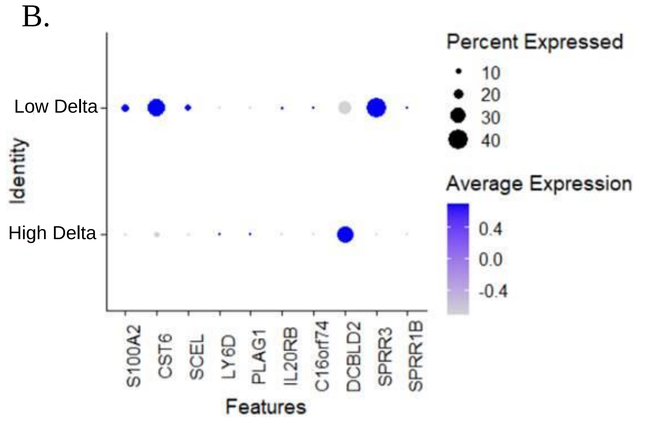

Figure 4. Average expression and percent expressed of known classical (A) and basal-like (B) gene markers in high and low delta tumors.

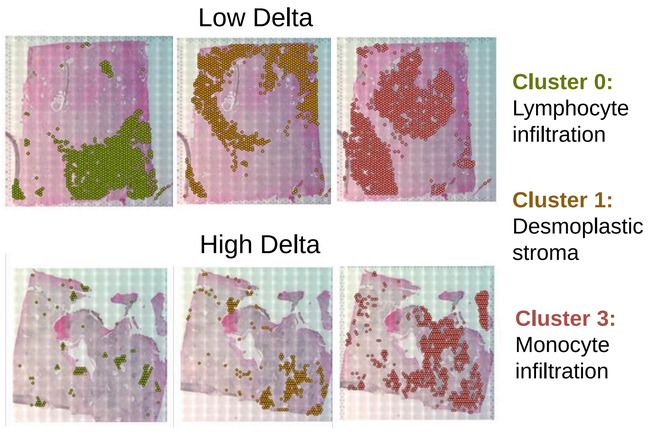

Figure 5. Correlation between genetic clusters and morphology.

Conclusions

Our preliminary data suggest potential differences in spatial transcriptional profiles and subtype marker expression between high and low delta tumors, which is vital information in developing treatment plans personalized for each patient. We will continue our analyses and validate results that may be actionable in clinic.

References

1) Hidalgo, N Engl J Med 2010; 362:1605-1617
2) Koay et al., *Clin Cancer Res* (2018) 24 (23): 5883–5894.
3) Juiz et al., Faseb. 2020;34(2):12214-12228