nanoString®

Spatial transcriptomic characterization of the *Gtf2i* LH24H KI mouse model of human thymoma
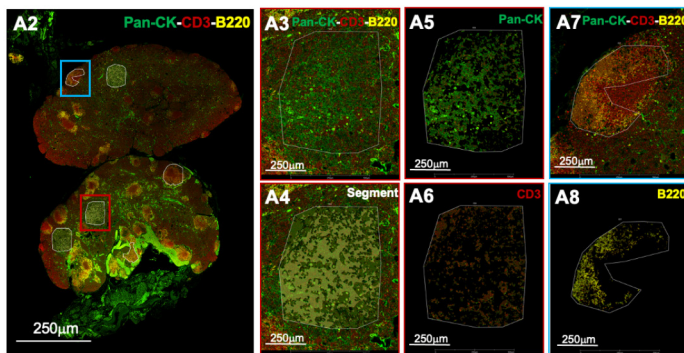
Background

- The pathogenesis of thymic epithelial tumors is not well understood and there is a lack of disease models
- *GTF2I* L424H is the most recurrent mutation in thymic tumors but its role in tumorigenesis is unknown

Research Question

What is the role of the *GTF2I* L424H mutation in thymic epithelial tumors?

Experimental Setup

Instrument	GeoMx® DSP
Sample Type	FFPE
Tissue Type	Thymus
Assay	Mouse Whole Transcriptome Atlas
Analyte	RNA
Readout	NGS

Why GeoMx?

Digital spatial profiling allowed for the thorough characterization of individual thymic lesions and medullary and cortical thymic epithelial tissue in a manner that could not be done with traditional sequencing.

Freeform ROIs were drawn in thymomas and medullary/cortical epithelial tissue and then segmented based on PanCK, CD3, or B220 staining to profile epithelial cells, B cells, and T cells. Figure reproduced with permission from Elsevier from He et al. J Thorac Oncology 2022.

Results & Conclusions

- 113 positively enriched and 4 negatively enriched transcription factor gene sets in epithelial thymomas compared to medullary or cortical thymus epithelial tissue.

- Eight of the top 10 gene sets related to E2F – human B1 and B2 type thymomas are also enriched for this pathway

- Other enriched gene sets included MYC_targets_V1, E2F_targets, and G2M checkpoint. Negatively enriched gene sets include interferon alpha and gamma, inflammatory response, and TNFA signaling by NFKB

- Expression levels of Birc5, Top2a, Mki67, and Mcm family members were higher in thymoma ROIs than medullary or cortical ROIs, consistent with the enrichment of E2F and MYC pathways. There was also enrichment in PI3K-Akt-mTOR signaling and adipogenesis in thymoma ROIs.

- Thymomas are composed of heterogeneous epithelial cells that express genes associated with cortical TECs and thymic epithelial progenitor cells (TEPCs) and the *Gtf2i* L424H KI mice transcriptionally resemble human B1 and B2 type thymomas.

He Y et al. A Knock-In Mouse Model of Thymoma With the GTF2I L424H Mutation. J Thorac Oncol. 2022 Dec;17(12):1375-1386. © Elsevier
https://doi.org/10.1016/j.jtho.2022.08.008

For more information, please visit nanostring.com/geomx