Spatial Transcriptomics of Thoracic Aortic Pathology

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Background: Thoracic aortic pathology most commonly reviewed at our institution includes aortic aneurysms, acute dissection and acute aortitis, all which are associated with distinct histologic and morphologic features. Spatial transcriptomics enables visualization of individual cell types that correspond to a specific molecular signature, providing valuable insight into the pathogenesis of aortic disease.

Methods: Using human aortic tissue from three separate subjects who underwent repair for an enlarging thoracic aortic aneurysm, acute aortic dissection and acute aortitis, the 10x Genomics Visium platform using the GeoMx digital spatial profiler and single-nucleus RNA sequencing were completed to identify gene expression signatures within single cells and map distinct cellular populations.

Results: Significantly upregulated molecular signatures within pathogenic cell clusters within the aortic intima, media and adventitial layers (including the vaso-vasorum, lymphoid aggregates and peripheral nerve bundles) were identified within 7 annotated cell clusters. In aortic dissection tissue, cluster 1 composed of cells within the medial layer showed IGFBP3 was most upregulated (p= 2.8601E-60). The same cluster for aortic aneurysmal and active aortitis tissues revealed APOD (p=6.286E-230) and HSPB7 (p=2.574E-142) were most significantly increased, respectively (see Table 1 for full list).

	Aortic Dissection		**Aortic Aneurysm**		**Aortitis**	
Cluster 1	**Gene**	**P-value**	**Gene**	**P-value**	**Gene**	**P-value**
	IGFBP3	2.8601E-60	*PI16*	1.60E-216	HSPB7	2.574E-142
	C3	1.9841E-53	*PLA2G2A*	4.63E-190	SUSD5	5.089E-135
	FLNC	2.4936E-52	*FBLN1*	7.650E-187	SOST	5.882E-126
	PLAT	2.7402E-50	*DCN*	1.591E-183	RAMP1	1.066E-113
	CRYAB	9.2681E-49	*C7*	1.591E-193	TPM2	1.104E-112

Conclusion: We provide a novel combined molecular-histologic map at the whole transcriptome level of common human aortic pathologies. These findings may facilitate discovery of future novel interventional targets with direct functional relevance for the diagnosis and treatment of thoracic aortic diseases.