Diabetic Complications Consortium

Application Title: Multi-scale imaging tools to map pathology and gene expression in the human kidney

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1. Project Accomplishments:

We have developed tools to evaluate the level of intra-kidney heterogeneity in gene expression in the context of the intact human kidney. We have performed stereotactic biopsy in over 30 kidneys donated to research (not accepted for transplantation), from both healthy and diabetic donors. We first evaluated the level of spatial heterogeneity in pathology measured from biopsy. We then performed systematic biopsy to determine the relationship between gene expression and histopathology.

2. Specific Aims:

Aim 1: Measure heterogeneity in tissue pathology using MRI and site-directed stereotactic biopsy in the healthy and diabetic human kidney.

Results: We systematically biopsied >30 human kidneys three times each from three different locations. A blinded, board- certified pathologist scored the biopsy tissues and we evaluated the levels of glomerulosclerosis and fibrosis (IFTA) detected from each kidney. As shown in Figure 1, histopathology scores varied widely across biopsies from the same kidney. This was true regardless of kidney donor profile index (KDPI). We conclude that there is a high level of heterogeneity in pathology in the human kidney that is likely mirrored in spatially variable patterns in gene expression.

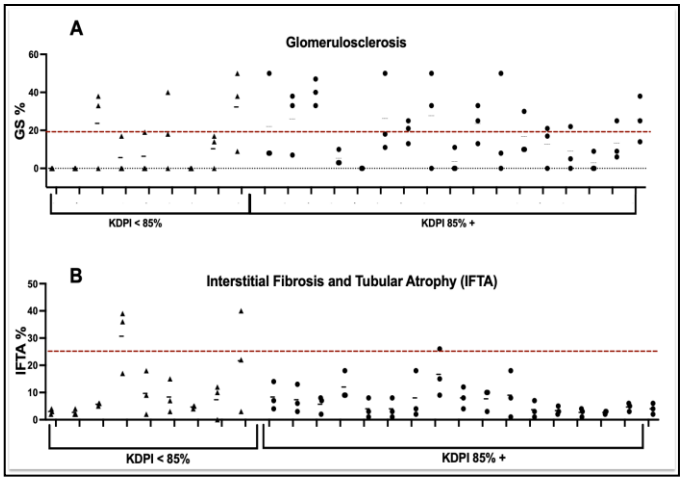

Figure 1: Diagnosis and pathology scores from biopsy are highly spatially variable.. X axis indicates individual humank kidneys, with three biopsies per kidney. Scores varied by up to 90% within each kidney, and variability occurred independent of KDPI.

Aim 2: Map gene expression across the kidney and correlate transcriptomics with tissue microstructure from MRI.

We have collected samples across the human kidney to measure variability in gene expression and its relationship to spatially- coincident pathology. Results are pending.

3. Publications:

Publications pending.