Exploring the Pathogenesis of Diabetic Kidney Disease (DKD) Progression by Urinary Single-Cell RNA Sequencing

ISN INTERNATIONAL SOCIETY OF NEPHROLOGY

Background

scRNAseq technology:

Gene expression at a single-cell level

Provides insights on subpopulations of cells & their roles in disease progression

Prognostic biomarker in early DKD

Urinary exfoliated kidney cells

Non-invasive biomarkers for DKD prognostication

Aim

Utility of urinary scRNAseq in determining the pathogenesis of DKD progression over time for optimization of therapy

Methods

baseline

Adults with early DKD

eGFR 60-90ml/min/1.73m2

800-1000ml of urine were collected

Urinary exfoliated kidney cells

Washed, collected, labelled with barcoding antibodies

Stained with viability dyes

The same number of viable cells from each sample were sorted by an INCYTO hemocytometer

BD Rhapsody Single Cell Analysis System & bioinformatics analyses

Results

n=8 DKD

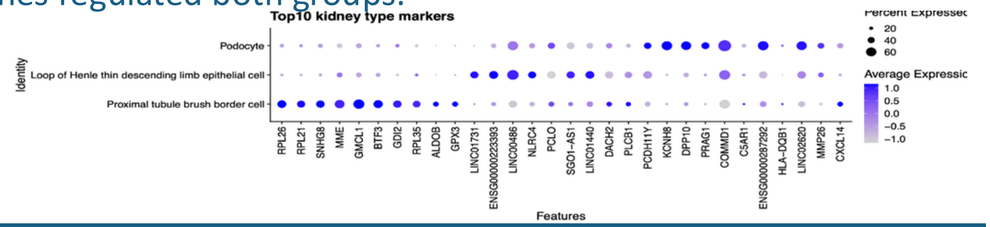
n=4 Progressive vs n=4 non-progressive

Numerous kidney,hematopoietic & epithelial cell types were identified:

Predominant cell: **20%** PTCs

Exfoliated more PTCs **p<0.05** Exfoliated Less PTCs

scRNAseq analysis of the urinary cells elucidated genes expressed & genes regulated both groups:



Signaling pathways that are significantly regulated between the 2 groups were identified:

Mitochondrial &amp Metabolic pathways (PPAR signaling & toll-like receptors)

Inflammation pathways (IFNγ, IL-6, Activator Protein-1 which modulate NF-κB activity)

Oxidative stress

Fibrosis pathways (TGFB & amp &SMAD)

scRNAseq, single -cell RNA sequencing; PTCs, Proximal tubule cells; progressive or non progressive group was defined as per the KDIGO 2024 guideline

Conclusion: scRNAseq of urinary cells is a viable, non-invasive method to monitor DKD. Progressive DKD patients can be distinguished from non-progressive patients by a significantly higher exfoliation of PTCs and distinct genetic signatures. Disease progression is driven by measurable changes in mitochondrial, oxidative stress, fibrosis, inflammation, and metabolic pathways.

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