Cell profiling defines metabolic dysregulation in kidney fibrosis

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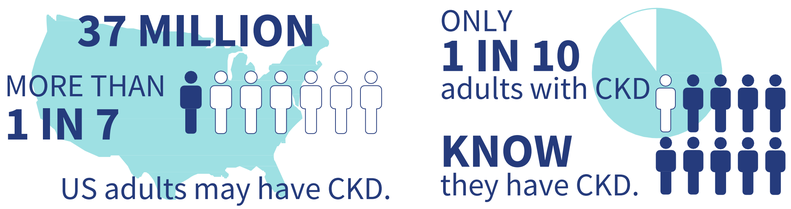
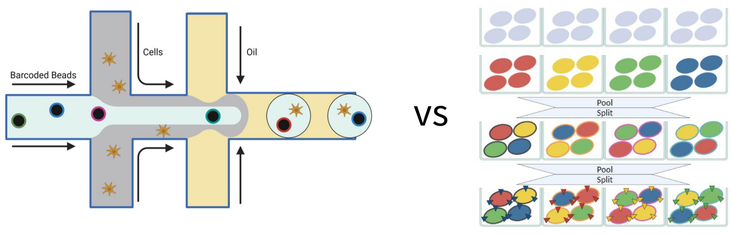
INTRODUCTION

Chronic Kidney Disease (CKD)



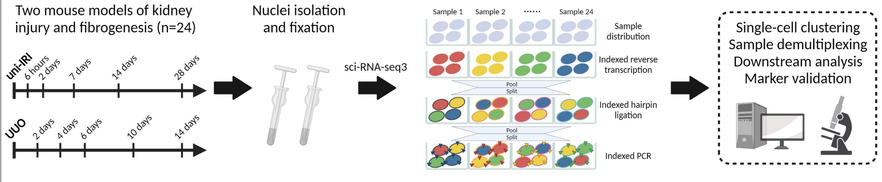
Q1: What's the earliest cellular event driving kidney fibrosis?
Q2: What's the mechanism driving metabolic dysregulation?

Single-cell RNA sequencing (scRNA-seq)



Current popular scRNA-seq platforms have **limitations** including throughput, sample multiplexing ability, batch effects and costs.

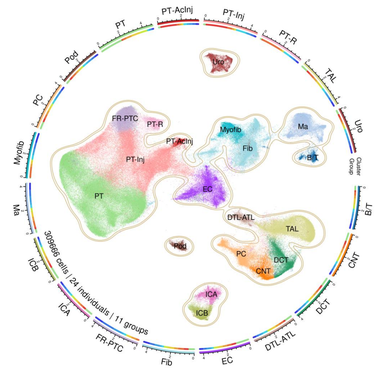
METHODS & WORKFLOW



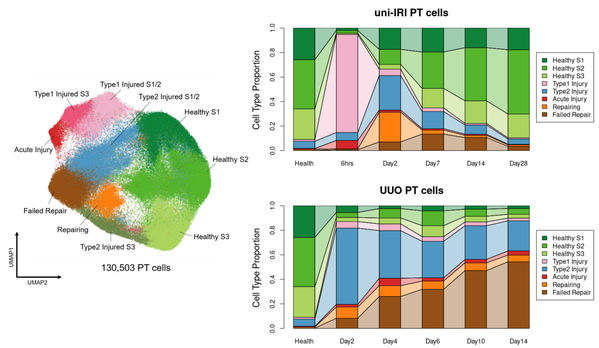
We leveraged the high throughput, high sample multiplexing capacity, and low costs of **sci-RNA-seq3** to characterize two mouse models of kidney injury and fibrosis (IRI/UUO) at multiple time points (a total of 24 samples).

RESULTS

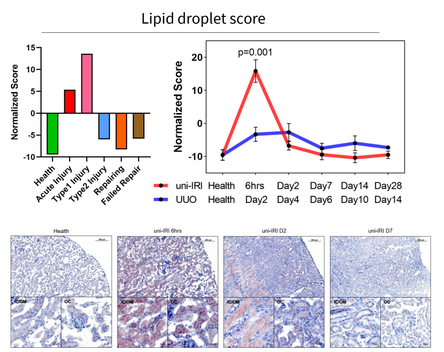
1. Over 300K cells from 24 samples profiled in a single experiment with reduced batch effects and low costs



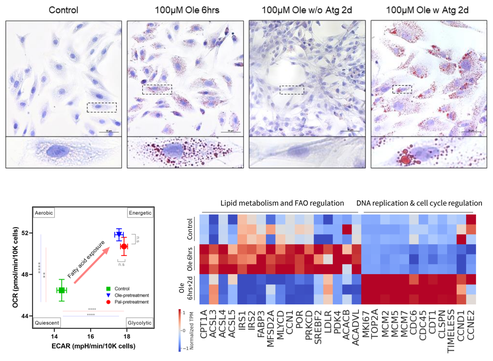
2. Two novel cell states of proximal tubular (PT) cells identified at early stages of fibrosis



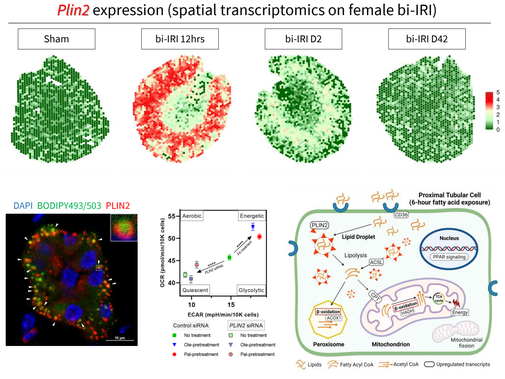
3. Transient lipid accumulation in PT cells at early stage of IRI



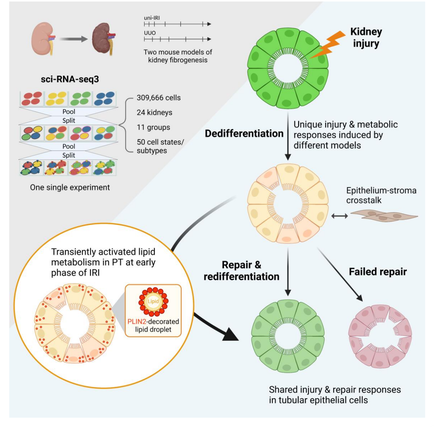
4. Increased fatty acid oxidation during lipid accumulation in PT



5. PLIN2 is identified as a marker of lipid droplets and important for energy state maintenance.



6. A unique scRNA-seq resource of kidney fibrosis



CONCLUSION & ACKNOWLEDGEMENT

- sci-RNA-seq3 profiles 309,666 cells from 24 mouse kidneys in a single experiment
- Two cell states of injured proximal tubule have different metabolic signature
- Transiently activated lipid metabolism and PLIN2+ lipid droplets in early IRI
- Shared and unique injury and repair responses across the nephron tubule

The Humphreys Lab

DBBS Graduate Program

Work accepted by Cell Metabolism