

# Direct Reprogramming of Fibroblasts to induced Renal Tubule Cells (iRECs)

For *in vitro* disease modeling or nephrotoxicity testing

## Technology

Direct reprogramming by forced expression of transcription factors can convert one cell type into another. Thus, desired cell types can be generated bypassing pluripotency. However, direct reprogramming towards renal cells remains an unmet challenge. We identified four renal cell fate inducing factors and demonstrate that their combined expression converts mouse and human fibroblasts into induced renal tubular epithelial cells (iRECs). iRECs exhibit epithelial features, a global gene expression profile resembling their native counterparts, functional properties of differentiated renal tubule cells and sensitivity to nephrotoxic substances. Furthermore, iRECs integrate into kidney organoids and form tubules in decellularized kidneys. Our approach demonstrates that reprogramming factors can be identified by targeted *in silico* analysis. Renal tubular epithelial cells generated *ex vivo* by forced expression of transcription factors may facilitate disease modelling, drug and nephrotoxicity testing, and regenerative approaches.

### Innovation

- Direct reprogramming from fibroblasts to renal tubule cells
- Replicate essential features of native tubule cells
- No pluripotency or iPS reprogramming necessary
- Long term culture and propagation possible
- High sensitivity to known nephrotoxins

### Application

- Nephrotoxicity testing of novel compounds
- *In vitro* modelling of human renal diseases
  - ADPKD, tubulopathies, nephrolithiasis
  - Infections (BK-virus)
- Drug response testing in tubule cells of desired genetic background

### Developmental Status

- Proof of principle for reprogramming of mouse and human cells
- Application to disease modeling in progress
- Further refinement of cell type specificity in progress

### Responsible Scientist

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### Branch

Pharma, Biotech

### Patent Status

PCT patent application pending  
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