NEWCELLS
IN VITRO MODELS TO PREDICT *IN VIVO* OUTCOMES

Glomerular podocyte assays for renal drug safety/efficacy testing and disease modelling

Assessment of podocyte damage biomarkers and podocyte permeability

Achieve:

- Reliable predictive glomerulus toxicology data to support drug discovery programs
- Podocyte injury and Proteinuria, Fibrosis or Diabetes modelled *in vitro*

What you can expect:

- Use of fully differentiated and characterised primary podocytes
- Rapid assay turnaround time

Modelling the glomerular filtration barrier (GFB) to achieve predictive results

Being able to reliably reproduce the glomerular filtration barrier *in vitro* provides the basis for toxicity screening and disease modelling allowing to confidently progress studies *in vivo*.

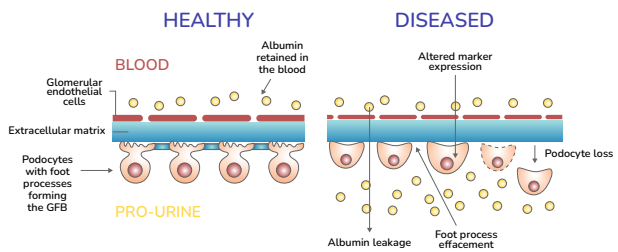

Figure 1: Schematic representation of what happens to the glomerular filtration barrier upon loss of function.

Glomerular toxicity evaluation

Damage to podocytes as well as large molecule leakage through the GFB has been assessed in our model following exposure to the toxic agent Adriamycin. Increasing exposure of podocytes to Adriamycin leads to a reduced transepithelial electrical resistance and increased GFB permeability. Changes in permeability are assesed by quantifying large molecule (dextran) leakage across the GFB modelling proteinuria occuring *in vivo* and by measuring cell viability. **(Figure 2).**

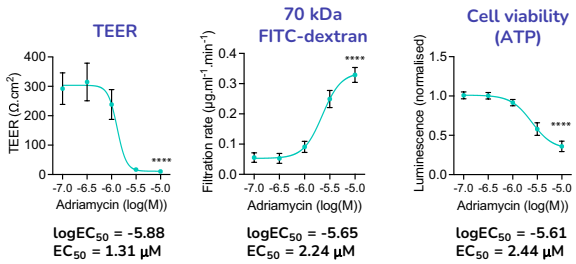

Figure 2: Example in house permeability assay data obtained following treatment of our podocyte model with the toxic agent Adriamycin.

Glomerular disease modelling

Fibrosis or diabetic nephropathy have also been modelled through exposure of podocytes to agents known to mimic these diseases, in particular TGF-β and palmitate respectively. Addition of palmitate fatty acid recapitulates a lipid-rich environment within the glomerulus, mimicking phenotypic changes seen in diabetic patients with damaged GFB and increased protein levels in urine due to resulting protein leakage. The damage also correlates with reduced cell viability quantified in an ATP assay. **(Figure 3).**

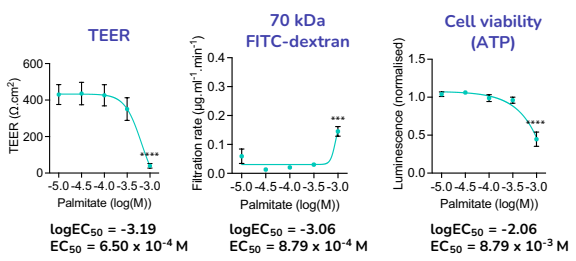

Figure 3: Typical permeability assay results seen in the diabetes model induced upon exposure of podocytes to nephrotoxic.

NEWCELLS
IN VITRO MODELS TO PREDICT IN VIVO OUTCOMES

Primary podocytes for a more predictive environment

Using primary podocytes ensures that experiments are carried out in an environment that most closely mimics the *in vivo* one with higher expression levels of podocyte-specific markers and rigourous formation of tight junctions when compared to commonly-used immortalised podocytes **(Figure 4 and Figure 5).**

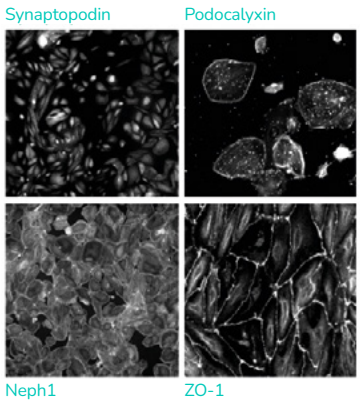

Figure 4: Immunofluoresence staining of primary podocytes expressing Synaptopodin, Podocalyxin, Neph1 and ZO-1 tight junction protein.

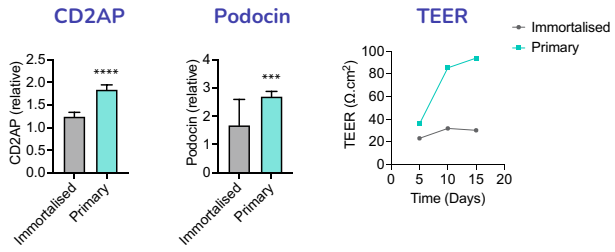

Figure 5: Phenotypic comparison of primary podocytes and immortalised podocytes. Podocyte marker Podocin, CD2AP and Nephrin levels are lower in immortalised podocytes. Similarly, the TEER is also reduced suggesting higher membrane permeability compared to primary podocyte.

Available assays and readouts	
Glomerular toxicity assays	TEER, ATP, 70kDa FITC Dextran permeability, Imaging
Podocyte injury assay	IL-6, MCP-1. LDH
Disease modelling	Available for focal segmental glomerlosclerosis (FSGS) and diabetic nephropathy
High content imaging	Matrix deposition, ECM, collagen, fibronectin, cell death, ER stress

Newcells Biotech

The Biosphere, Draymans Way, Newcastle Helix
Newcastle Upon Tyne, NE4 5BX

+44 (0)191 580 6184 | enquiries@newcellsbiotech.co.uk