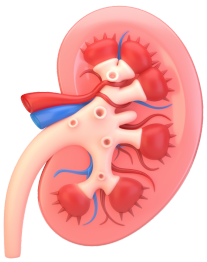
aProximate™ Kidney Technical Sheet



NEWCELLS
BEST BIOLOGY DRIVING *IN VITRO* INNOVATION

Product Information

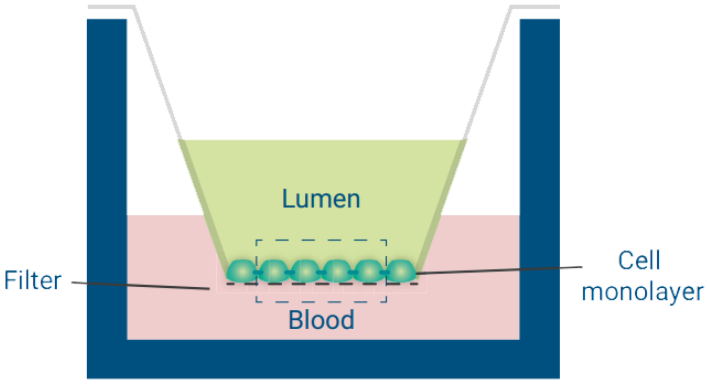
aProximate™ is Newcells' *in vitro*, pre-clinical renal proximal tubule cell (PTC) assay that accurately reflects the functional characteristics of the human nephron.

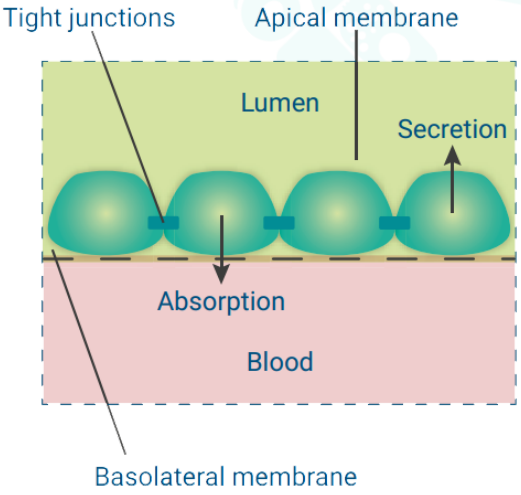
aProximate™ is a unique primary cell *in vitro* system for investigating renal drug handling, drug-transporter interactions, drug safety and transporter-mediated drug-drug interactions.

The *in vivo* renal proximal tubule epithelia is a specialised polarised cell layer in the kidney that is a major site of drug secretion and absorption, mediated by membrane located transporters.

aProximate™ is a monolayer assay that effectively recreates the architecture of polarised PTC on a semipermeable membrane, recapitulating the *in vivo* epithelium. aProximate™ expresses all major transporter proteins at higher levels compared to other commercially available *in vitro* systems.

aProximate™ presents a near-physiological model which maintains the full complement and expression level of endogenous renal transporters. Therefore aProximate™ provides a robust, predictive tool for renal transport and safety studies, relevant to clinical studies





Kidney PTC are isolated from the cortex of fresh, healthy kidney and seeded on permeable filter HTS Transwell™ membranes where they form a polarised confluent monolayer with tight junctions that allows the addition of test compounds to the apical or basal sides of the tubule. The model can be generated from a range of species, allowing rapid cross-species analysis for pre-clincial studies.

GET IN TOUCH WITH THE TEAM FOR FURTHER INFORMATION

Call us on +44 (0)191 580 6184
Or email us at enquiries@newcellsbiotech.co.uk
Or via our contact form newcellsbiotech.co.uk/contact-us

How you can use the aProximate™ model

- ✓ Identification of transporter-mediated renal drug clearance pathways for xenobiotics during drug development
- ✓ Identification of clinically important transporter-mediated Drug-Drug Interactions during drug development and post market in clinic
- ✓ Identification of cross species differences in renal drug handling - de risking adverse outcomes at first in man
- ✓ Application of renal model to identify renal target and target engagement/efficacy
- ✓ Development of screening regime for biologics transport and toxicity
- ✓ Identification of drug induced kidney damage using clinically relevant biomarkers of nephrotoxicity cross species as a predictive tool to improve 'first in man' outcomes.

aProximate™ Primary Tubule Cells remain extremely well differentiated

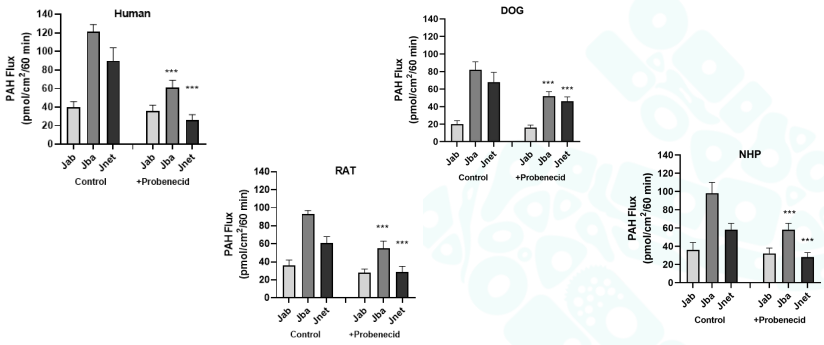
Key Transporter Expression

Gene	Percentage of native kidney expression			
	aProximate™	HK2	REPTEC	HEPTEC
MDR1	65.2 ± 7.1	34	26	28.1
BCRP	31.3 ± 5.5	ND	TBC	TBC
MRP2	31.5 ± 33	1	6	7
MRP4	29.3 ± 4.8	26	24	81
OAT1	20.6 ± 4.6	ND	ND	ND
OAT3	27.8 ± 6.7	ND	ND	ND
OCT2	39.7. ± 4.3	ND	1.8	3.3
OATP4C1	39.0 ± 2.7	28	34	47.6
SLC2A9	27.7 ± 4.8	ND	ND	ND
URAT1	34.6 ± 9.2	ND	ND	ND
MATE1	36.4 ± 4.2	ND	0.6	0.1
MATE2K	15.1 ± 8.8	ND	0.3	ND

aProximate™ outperforms competition

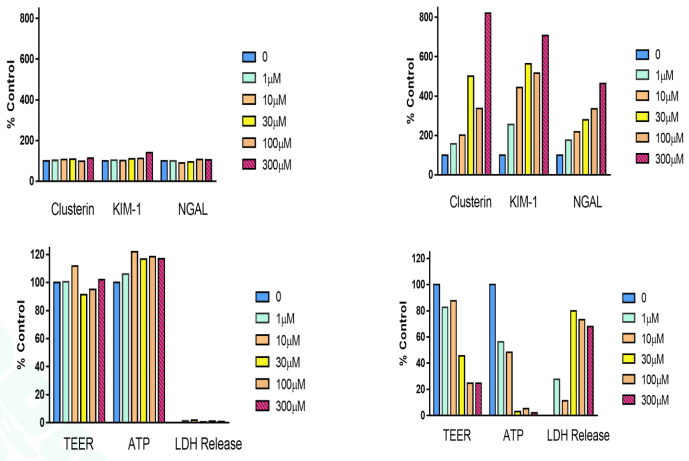
Cross Species Handling of PAH (Para-aminohippurate)

Transcellular flux: Absorptive and Secretory
Paracellular flux: Using mannitol or Lucifer yellow we can differentiate between leak and transporter-mediated transport
Net transport: Drug molecule secretion and accumulation
Transporter-mediated Drug-Drug Interactions: By the addition of known inhibitors, we can identify potential transporter-mediated drug-drug interactions



Qualification of the aProximate™ model as predictive of kidney injury

- ✓ Some compounds cause toxicity to PTCs and lead to kidney damage (drug induced kidney injury - DIKI).
- ✓ Serum biomarkers, such as creatinine, are not sensitive enough to detect early DIKI.
- ✓ Kidney-specific biomarkers are much better indicators of early PTC damage.
- ✓ Many drugs are known to be toxic to PTCs but the mechanisms of toxicity are largely unknown.



Non toxic Drug

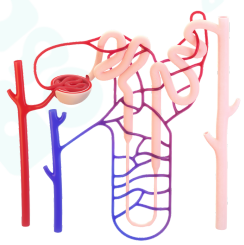
Nephrotoxic Drug

***In vitro* model – aProximate™ 36 compounds**

	Sens./Spec (%)	PPV/NPV (%)	LR+	OR	Max YI
With all endpoints	70.0/62.5	70.0/62.5	1.87	3.9	0.33
Only biomarkers	70.0/87.5	87.5/70	5.6	16.3	0.58
> 2 biomarkers	60.0/93.8	92.3/65.2	9.6	22.5	0.54

Bajaj et al., Toxicology (2020)

- ✓ Cell monolayer exposed to range of drug concentrations for 48 hours
- ✓ FDA approved biomarkers; Clusterin, NGAL and KIM-1 measured along with ATP production
- ✓ TEER and LDH release
- ✓ Very Predictive of *in vivo* outcome; 60%/93% Sens/Spec and 92.3% PPV and 65.2% NPV



NEWCELLS aProximate™ Kidney Model
https://newcellsbiotech.co.uk/models/

Visit our aProximate™ page

Newcells Biotech, The Biosphere, Draymans Way, Newcastle Helix, Newcastle Upon Tyne, NE4 5BX
T: +44 (0)191 580 6184 E: enquiries@newcellsbiotech.co.uk W: www.newcellsbiotech.co.uk