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aProximate™
TECHNICAL SHEET

PRODUCT INFORMATION

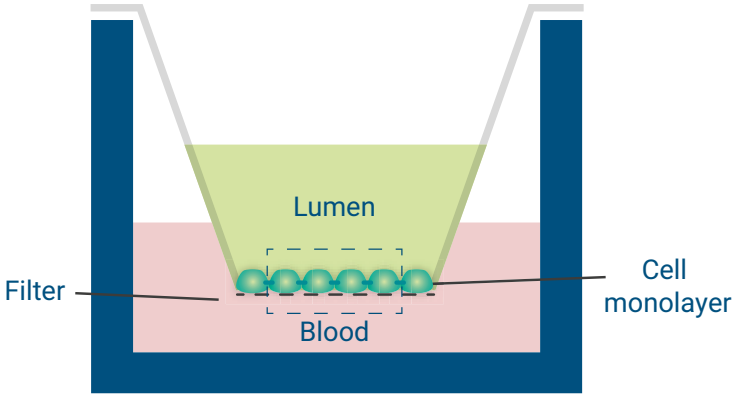
aProximate™ is Newcells Biotech's in vitro, pre-clinical renal proximal tubule cell (PTC) assay that accurately reflects the functional characteristics of the human nephron.

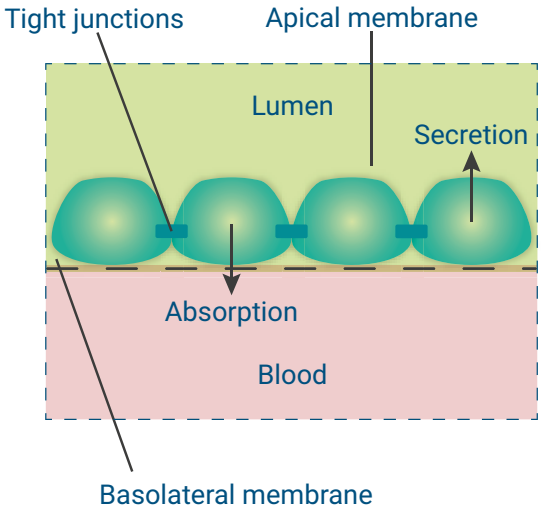
aProximate™ is a unique primary cell in vitro system for investigating renal drug handling, drug-transporter interactions, drug safety and transporter-mediated drug-drug interactions.

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.

APPLICATIONS

- Drug pharmacology renal transporters[1, 2]
- Drug-drug interactions[3]
- Renal safety prediction studies[2, 4, 5, 6]
- Species drug handling differences[2, 7]
- Small and large molecules
- Labelled or unlabelled compounds
- Investigation of post-market toxic effects

READOUTS

The following analyses can be performed by Newcells Biotech:

Transcellular flux:

- Absorptive flux
- Secretory flux

Paracellular flux:

- Using mannitol or Lucifer yellow, we can differentiate between leak and transporter-mediated transport

Net transport:

- Drug molecule net secretion
- Drug molecule accumulation

Transporter-mediated drug-drug interactions:

- By the addition of known inhibitors, we can identify potential transporter-mediated drug-drug interactions

Renal drug safety:

- Investigation of nephrotoxic potential using a panel of early damage biomarkers (see table)

SERVICE INFORMATION

Newcells Biotech offer a high quality and reliable service for compound screening. Our expert kidney scientists advise our customers to design custom studies that will deliver the data required to develop their programs. All our work is carried out in our UK-based laboratories, working closely with our customers.

Our assays are available as ready-to-use if our clients prefer to perform the studies themselves.

PRICING

Contact us for a quote

SPECIFICATIONS

Format	Transwell™ inserts	
Selected Key Renal Transporters	**Apical membrane** • MDR1 • MRP2 • MRP4 • URAT1 • BCRP • MATE • OAT4 • OCTN1 • OCTN2 • NaPi2a • Megalin • Cubulin Plus many more	**Basolateral membrane** • OAT1 • OAT2 • OAT3 • OCT2 • OCT3 • OATP4C1 • NBC • GLUT9 Plus many more
Species	• Human • Rat • Mouse • Canine • Non-human primate	
Biomarkers	**aProximate™ expresses and measures the FDA qualified clinical safety biomarkers:** • KIM-1 • NGAL • Clusterin • TEER • LDH • ATP	

GET IN TOUCH WITH THE TEAM FOR FURTHER INFORMATION

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Or use our contact form

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References

1. Kumar, V. Yin, J. Billington, S. Prasad, B. Brown, C. D. A. Wang, J. Unadkat, J. D. The Importance of Incorporating OCT2 Plasma Membrane Expression and Membrane Potential in IVIVE of Metformin Renal Secretory Clearance. Drug Metabolism and Disposition. 2018;46(10):1441-1445 **2.** Brown, C. Development of a novel predictive in vitro non human primate proximal tubule model for drug transporter and nephrotoxicity studies. Drug Metabolism and Pharmacokinetics. 2019;34(1):S53 **3.** Chaudhry, A. Chung, G. Lynn, A. Yalvigi, A. Brown, C. Ellens, H. O'Connor, M. Derivation of a System-Independent Ki for P-glycoprotein Mediated Digoxin Transport from System-Dependent IC50 Data. Drug Metabolism and Disposition. 2018;46(3): 279-290 **4.** Bajaj, P. Chung, G. Pye, K. Yukawa, T. Imanishi, A. Takai, Y. Brown, C. Wagoner, M. P. Freshly isolated primary human proximal tubule cells as an in vitro model for the detection of renal tubular toxicity. Toxicology. 2020;422: 152535 **5.** Brown, C. Chung, G. Nicholds, M. Armstrong, L. Characterization of cisplatin toxicity in aProximate™ human proximal tubule cell monolayers. Drug Metabolism and Pharmacokinetics. 2019;34(1):S52-S53 **6.** Pye K, Chung G, Armstrong L, Nicholds M, Brown C. aProximate™ as a novel, predictive model of aminoglycoside-induced nephrotoxicity. Abstracts of the 55th Congress of the European Societies of Toxicology (EUROTOX 2019) TOXICOLOGY SCIENCE PROVIDING SOLUTIONS. Toxicology Letters. 2019;314:S167–8. **7.** Corvaro M. Bartels M. Brown C. Chung G. Chan M. An inter-species comparison of the triclopyr in vitro and in vivo toxicokinetic properties, for risk assessment purpose. Poster presented at: Society of Toxicology Annual Meeting; 2019; Baltimore, USA.