


A novel ready-to-use system for in vitro drug transporter evaluation

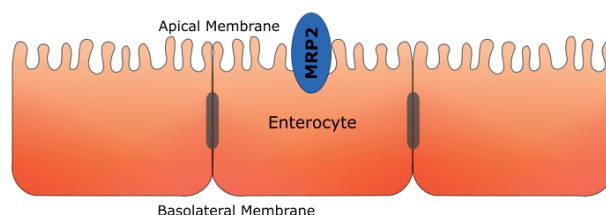
READYCELL INTRODUCES PREADYCTIVE MRP2 - IN COLLABORATION WITH NETHERLANDS CANCER INSTITUTE (NKI)



Monolayer assays using transfected MDCKII cells have been widely recognized tools to study the interaction of drugs with cellular transporters. Preadyctive-MRP2 is an in vitro model based on transfected MDCKII. Preadyctive-MRP2 is ready-to-use and consists of a tissue culture 24-plate seeded with transfected cells expressing MRP2 transporter as well as parental control cells.

Preadyctive MRP2 Applications

- Substrates assessments (direct transport studies)
- Inhibition assessment (drug-drug interaction)
- Models the net active transport event of barriers like the human intestinal epithelium, liver and kidney



MRP2 (ABCC2 gene) is mainly localized in the apical membrane domain of polarized cells such as hepatocytes, renal proximal tubule cells, and intestinal epithelia, mediating unidirectional transport of substrates to the luminal side of the organ.

Four simple steps to use Preadyctive



#1
Receive

Ready-to-use
Cell Barrier



#2
Liquefy

Liquefying of Solid
Shipping Medium



#3
Apply

Incubation with
Test Compound



#4
Assay

Assessment of
Permeability/Transport
End Point

Preadyctive MRP2 Benefits

- Available on demand under a limited Single-Use License
- Ready-to-use without in-house cell line development or acquisition and cell propagation
- Transportation and storage at room temperature in proprietary Shipping Medium
- Adaptable to HTS automation, assay protocols and plate layouts
- User friendly and easy-handling system
- High reproducibility

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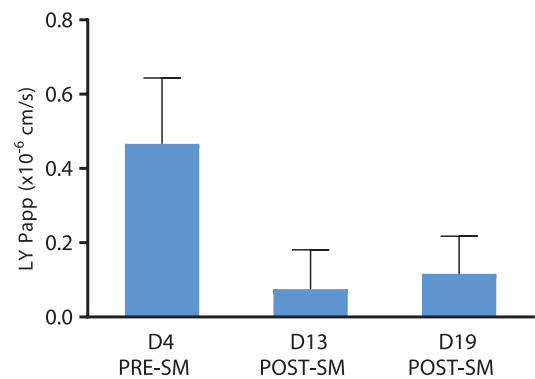
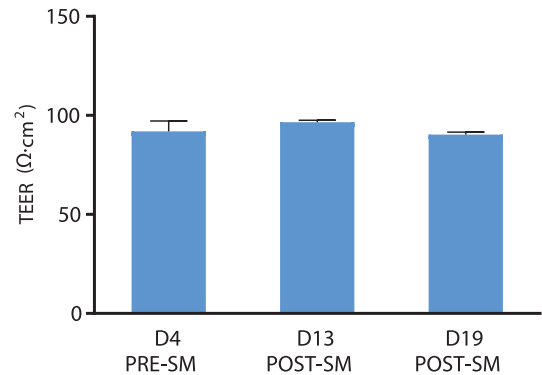
EXPERIMENTAL DATA

Stability of Preadyactive-MRP2 barrier

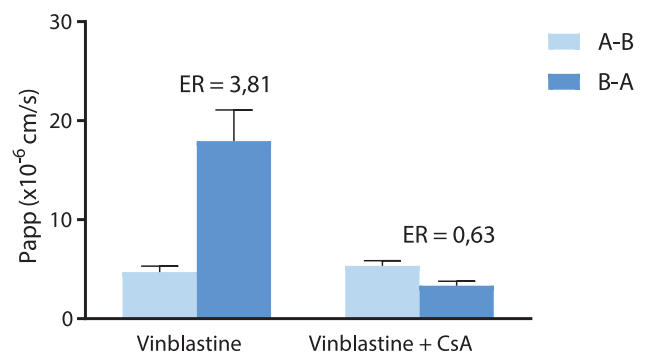
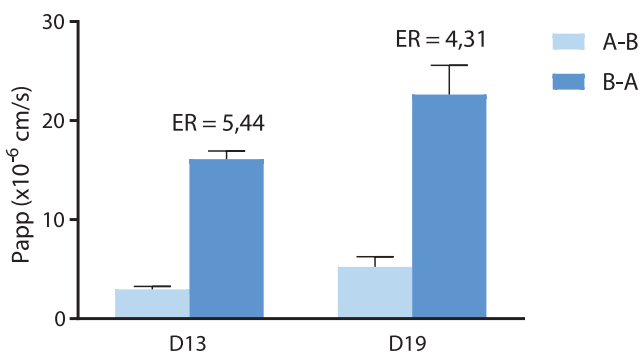
Quality Controls before and after Shipment

TEER was measured before shipping medium addition (D4). Immobilization was maintained for 4 days at room temperature. The shipping medium was then removed and TEER was measured after 5 days (D13) and 11 days (D19) standard culture conditions.

LY was measured before shipping medium addition (D4). Immobilization was maintained for 4 days at room temperature. The shipping medium was then removed and LY was measured after 5 days (D13) and 11 days (D19) standard culture conditions.



Permeability values and Efflux Ratio: Vinblastine-MRP2 substrate



MRP2-mediated Vinblastine transport was determined using Preadyactive-MRP2 kit at days D13 and D19 of culture. During substrate incubation, was also included Probenecid (MRP2 expression stimulator) and Elacridar (P-gp inhibitor).

Cyclosporine A (CsA) was used as MRP2 inhibitor in order to blockage MRP2-mediated Vinblastine transport activity.

MRP2 – Regulatory Requirements

Although there are several identified substrates and inhibitors of human MRP2 and different clinical citations on DDI, there is no specific recommendation for this transporter in the current FDA or EMA guidelines. Nevertheless, in vitro evaluation of the interactions of NCEs and particularly their conjugated metabolites should be considered on a case-by-case basis.