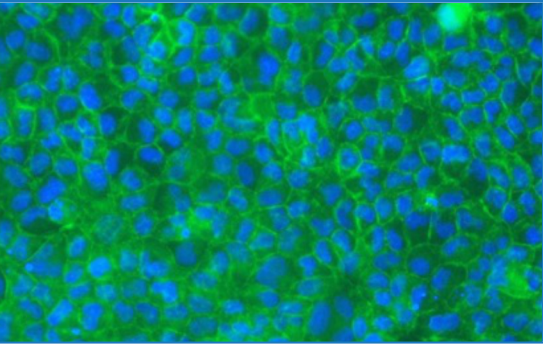


ReadyCell introduces PreadyPort-BCRP

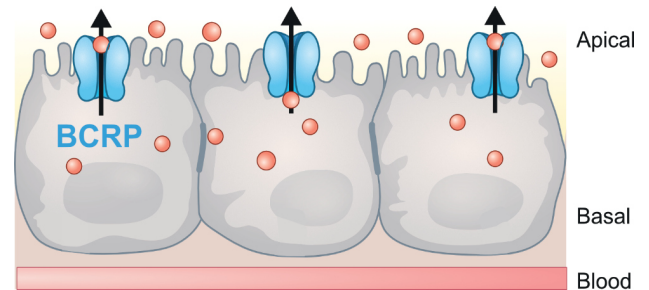


PreadyPort-BCRP is a cell-based assay for evaluating carrier-mediated transport in preclinical drug testing. It is delivered at room temperature in a semisolid shipping medium in Transwell-96 insert plates. The plate contains differentiated Mardin Darby Canine Kidney Type II (MDCKII) cell monolayers overexpressing the Breast Cancer Resistance Protein (BCRP) and/or the empty vector, according to the assay requirements.

PreadyPort-BCRP applications

The *BCRP*-expressing *MDCKII* cells model net drug efflux in expressed organs, identifying:

- ⦿ BCRP substrates, inhibitors and inducers
- ⦿ BCRP transporter-based drug drug interactions (concomitantly administered drugs)
- ⦿ Assay drug permeability by passive diffusion through a physiologically relevant barrier



The BCRP efflux transporter is localized in the apical cell membrane of barrier tissues (e.g. intestine, blood-brain barrier (BBB), placenta, and liver canalicular membrane) and excretory organs (bile and kidney) pumping compounds out of the cells. Substrates and inhibitors of BCRP include a wide range of clinically important and structurally diverse drugs and endogenous molecules^{1,2}.

Four simple steps to use PreadyPort-BCRP



#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

- ⦿ Available on demand, adaptive to project schedule
- ⦿ Worldwide room temperature shipments thanks to proprietary technology
- ⦿ Ready-to-use format, reducing costs and easing the assay procedure
- ⦿ Highest quality for a perfect replicability
- ⦿ Adaptable to automation
- ⦿ Specialized support from an experienced team

¹ Quingcheng M and Jashvant DU. Role of the breast cancer resistance protein (BCRP/ABCG2) in drug transport-an update, 2015, AAPS J 17:65-82.

² Feng B et al. Validation of human MDR1-MDCK and BCRP-MDCK cell lines to improve the prediction of brain penetration, 2019, J Pharm Sci, 108:2476-2483.

Experimental Data

Apparent Permeability (P_{app}) values and efflux ratios (ER) for the BCRP substrates, prazosin and dantrolene, in the absence/presence of Ko143, a reference inhibitor. Assays were performed after exposing *BCRP*-overexpressing cells (**PreadyPort-BCRP**) and those expressing the empty vector (**PreadyPort-WT**) to the shipping medium during a 4-day period and a subsequent 72-h recovery in fresh culture medium. *These data are the result of three independent experiments.*

■ P_{app} A-B ■ P_{app} B-A

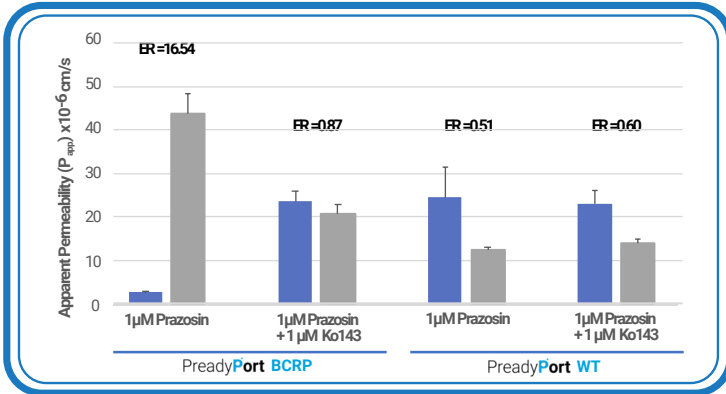


Figure 1. Prazosin secretory transport.

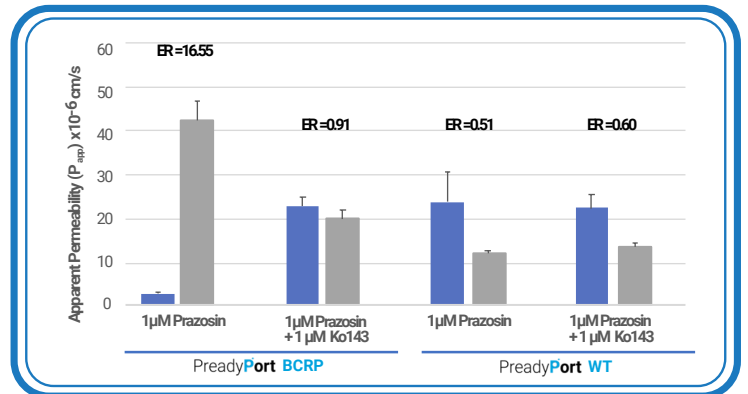


Figure 2. Prazosin secretory transport (batch-to-batch variation).

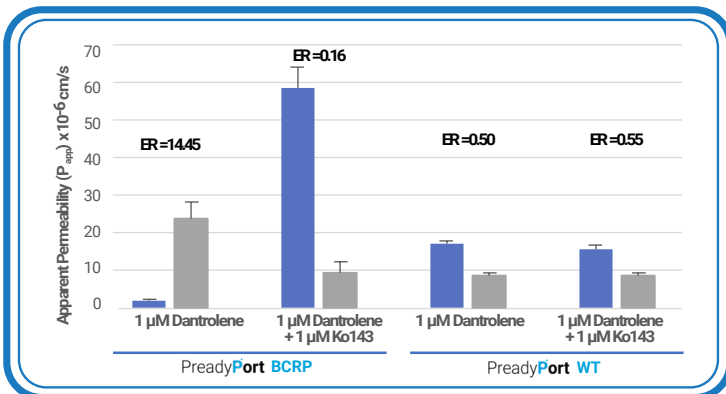


Figure 3. Dantrolene secretory transport.

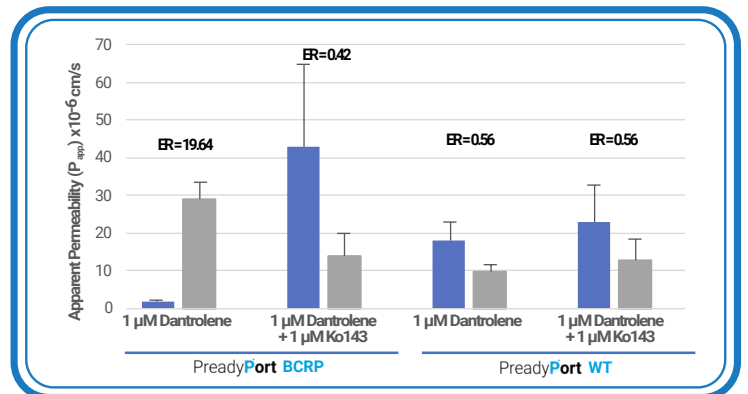


Figure 4. Dantrolene secretory transport (batch-to-batch variation).

Quality Controls

Pre- and post-assay quality assessments (TEER and Lucifer Yellow (LY), respectively) were performed to evaluate the cell barrier integrity of PreadyPort. TEER measurements were obtained 72 h after cell recovery from the shipping medium, while LY paracellular absorption was carried out after the sample permeability test.

■ PreadyPort WT ■ PreadyPort BCRP ■ LY Permeability ● LY Flux

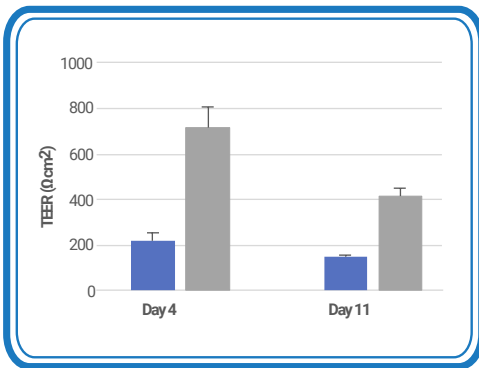


Figure 5. Changes in membrane integrity throughout the PreadyPort manufacturing process. *These data are the result of 3 different batches.*

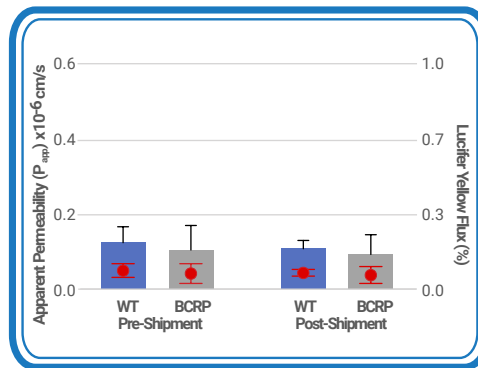


Figure 6. Lucifer Yellow paracellular permeability (P_{app}) values during PreadyPort shipment. *These data are the result of 3 different batches.*

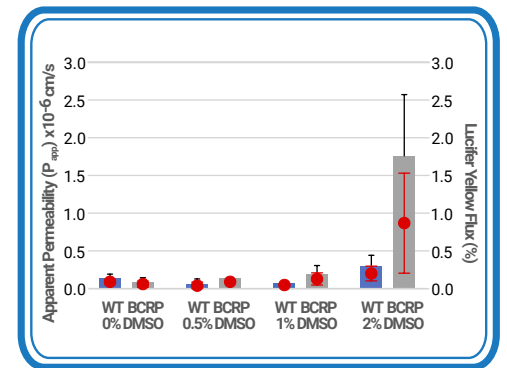


Figure 7. Effect of DMSO on barrier integrity of PreadyPort cell monolayers. *These data refer to a single experiment in triplicates.*

BCRP - Regulatory Requirements

Recommendations for identifying BCRP substrates and inhibitors are outlined by the 2020 FDA Guideline and recommended for consideration according to the 2012 EMA Guideline.