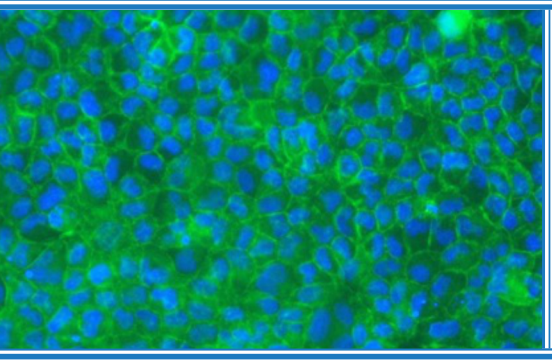
ReadyCell introduces PreadyPort-MDR1

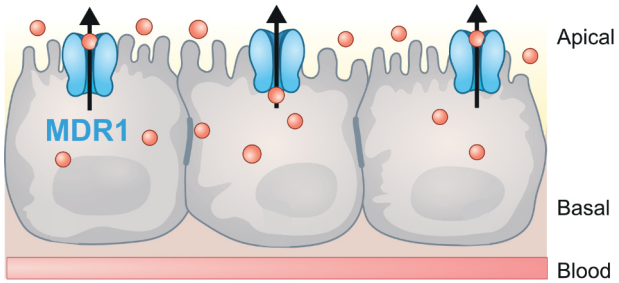


PreadyPort-MDR1 is a cell-based assay for evaluating carrier-mediated transport in preclinical drug testing. It is delivered at room temperature in a semisolid shipping medium in Transwell-96 insert plates. The plate contains differentiated Mardin Darby Canine Kidney Type II (MDCKII) cell monolayers overexpressing the Multidrug Resistance Protein 1 (MDR1) and/or the empty vector, according to the assay requirements.

PreadyPort-MDR1 applications

The *MDR1*-expressing *MDCKII* cells model net drug efflux in expressed organs, identifying:

- MDR1 substrates, inhibitors and inducers
- MDR1 transporter-based drug-drug interactions (concomitantly administered drugs)
- Assay drug permeability by passive diffusion through a physiologically relevant barrier



The MDR1 efflux transporter commonly referred to as P-glycoprotein (Pgp) is localized in the apical cell membrane of tissues such as intestine, testes, brain, and placenta, and excretory organs (bile and kidney) pumping compounds out of the cells. MDR1 has extremely wide substrate selectivity, preferentially transporting neutral or positively charged hydrophobic molecules[1,2]

Four simple steps to use PreadyPort-MDR1

#1 Receive	#2 Liquefy	#3 Apply	#4 Assay
Ready-to-use Cell Barrier	Liquefying of Solid Shipping Medium	Incubation with Test Compound	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

Seeling A. P-glycoprotein: one mechanism, many tasks and the consequences for pharmacotherapy of cancers, 2020, *Front Oncol*, 10:576559.
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.

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Experimental Data

Apparent Permeability (P_{app}) values and efflux ratios (ER) for the MDR1 substrates, digoxin and quinidine, in the absence/ presence of verapamil and valspodar, two reference inhibitors. Assays were performed after exposing *MDR1*-overexpressing cells (**PreadyPort-MDR1**) 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**

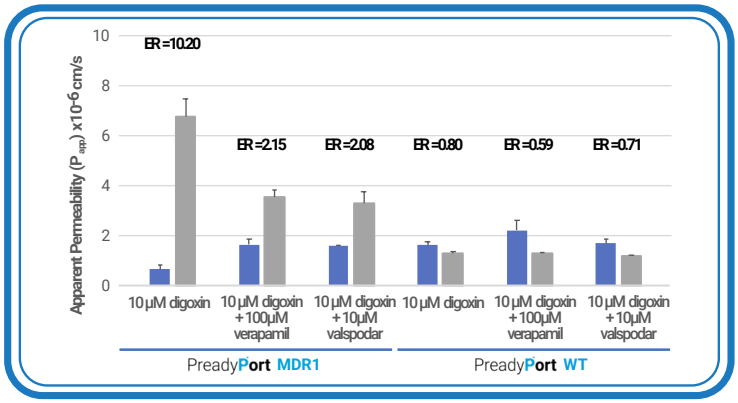

Figure 1. Digoxin secretory transport.

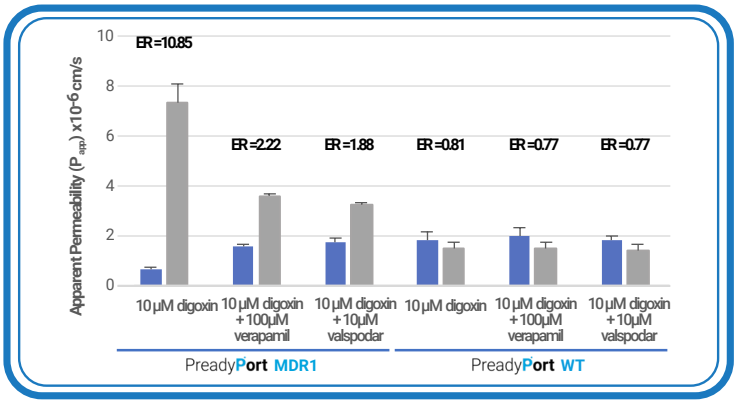

Figure 2. Digoxin secretory transport (batch-to-batch variation).

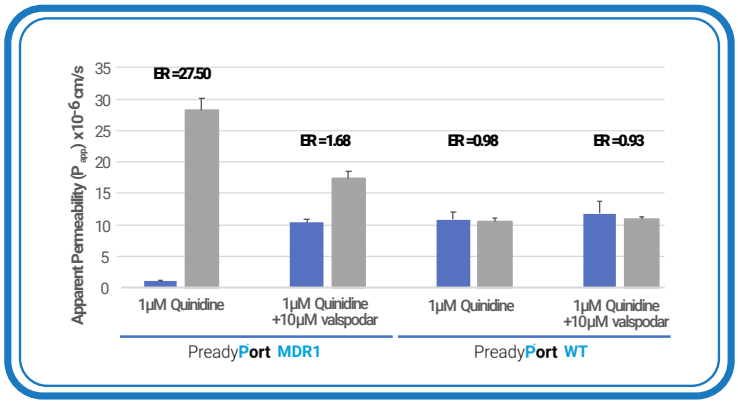

Figure 3. Quinidine secretory transport.

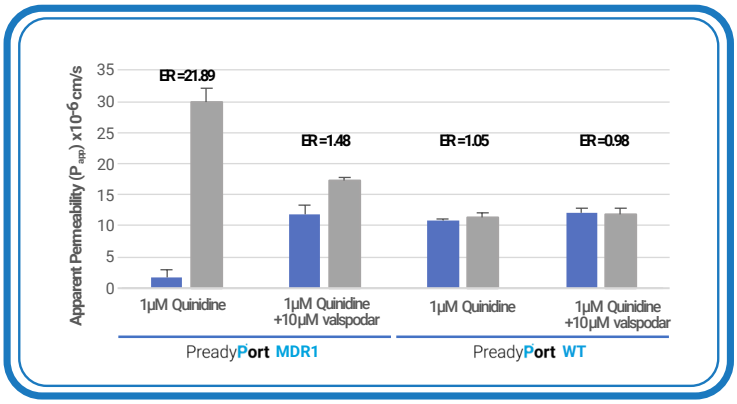

Figure 4. Quinidine secretory transport (batch-to-batch variation).

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 MDR1** ■ **LY Permeability** ● **LY Flux**

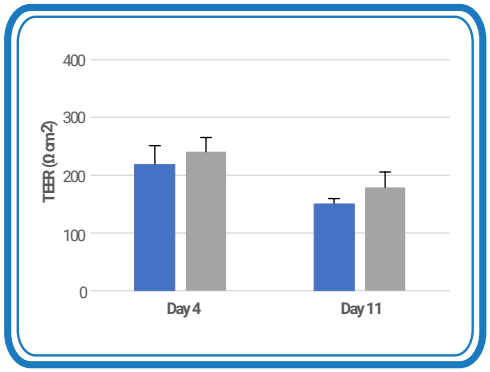

Figure 5. Changes in membrane integrity throughout the PreadyPort manufacturing process. *These data are the result of 3 different batches.*

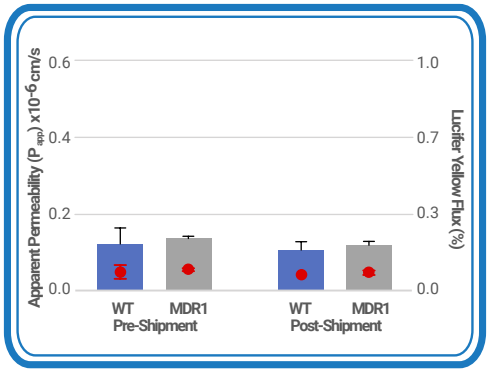

Figure 6. Lucifer Yellow paracellular permeability (P_{app}) values during PreadyPort shipment. *These data are the result of 3 different batches.*

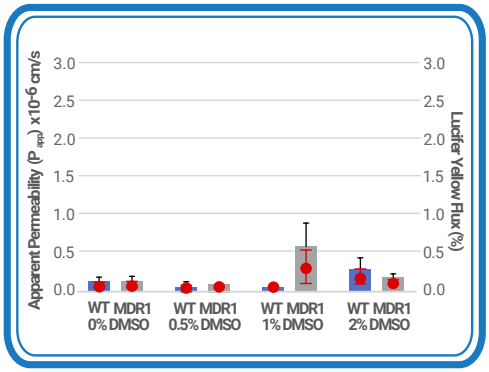

Figure 7. Effect of DMSO on barrier integrity of PreadyPort cell monolayers. *These data refer to a single experiment in triplicates.*

MDR1 - Regulatory Requirements

Recommendations for identifying MDR1 substrates and inhibitors are outlined by the 2020 FDA Guideline and recommended for consideration according to the 2012 EMA Guideline.