PreadyTake, an *in vitro* ready-to-use cell-based model to evaluate potential drug-transporter interactions

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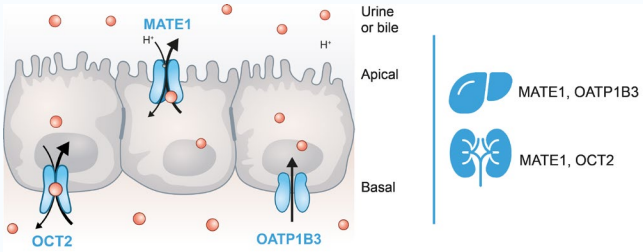
INTRODUCTION

Drug transporter proteins may compromise drug permeability across body barriers. Among the large number of transporters, **special attention** has been given to the **Solute Carrier Transporter (SLC) family** because of their role in the **renal and hepatic elimination of drugs.** Understanding the role of these transporters is normally performed *in vitro,* although tools are limited and may not reflect the true impact of a transporter on drug disposition. **PreadyTake** is a family of **ready-to-use** HEK293 **cell-based models individually expressing hepatic (OATP1B3), and renal (MATE1, OCT2) transporters** that emerges as useful tool **to evaluate potential drug-transporter interactions.**



Localization of the membrane-associated OCT2, MATE1 and OATP1B3 transporters in renal and hepatic cells.

OBJECTIVES

The main objective of this study is **to probe PreadyTake as an *in vitro* ready-to-use model to assess OATP1B3- MATE1- and OCT2-substrates, inhibitors and drug-transporter interactions.**

MATERIALS AND METHODS

Liquefaction and Shipping Medium Exchange

1. Liquify for 1,5h PreadyTake plate.

2. Aspirate Shipping Medium and add fresh HEK-293 medium.

3. Let cell recover for 72-h at 37°C.

Uptake Assay

1. Aspirate culture medium and wash with HBSS buffer. Repeat 2 times.

2. Add compounds to be tested, incubate at 37°C and wash with ice-cold HBSS buffer.

3. Lyse the cells with NaOH and neutralize with HCl. Centrifuge, collect supernatants and anlyze compound uptake by LC-MS.

RESULTS

Data were in compliance with FDA guidelines on drug-transporter interactions. Reference compounds **uptake were at least two-fold** that of cell expressing the empty vector (HEK293-MOCK). Furthermore, **absorption decreased by more than 50%** when reference compounds were incubated **in the presence of transporter inhibitors.**

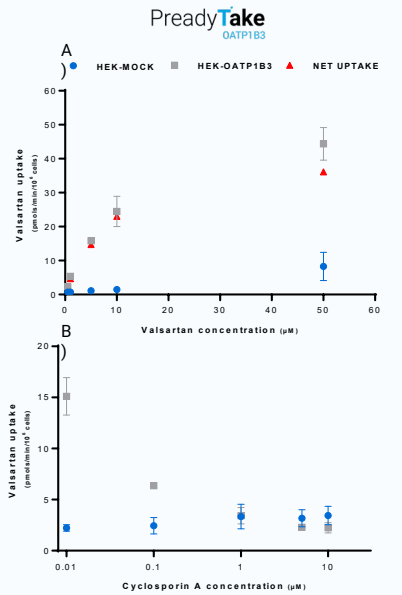


Figure 1. OATP1B3-mediated valsartan internalization in the absence (Panel A) or presence (Panel B) of cyclosporin A, an OATP1B3 inhibitor.

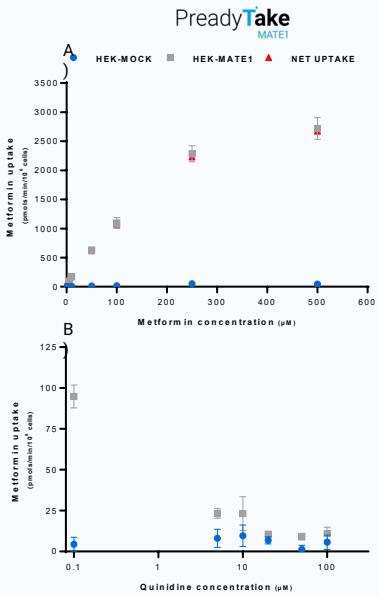


Figure 2. MATE1-mediated metformin internalization in the absence (Panel A) or presence (Panel B) of quinidine, a MATE1 inhibitor.

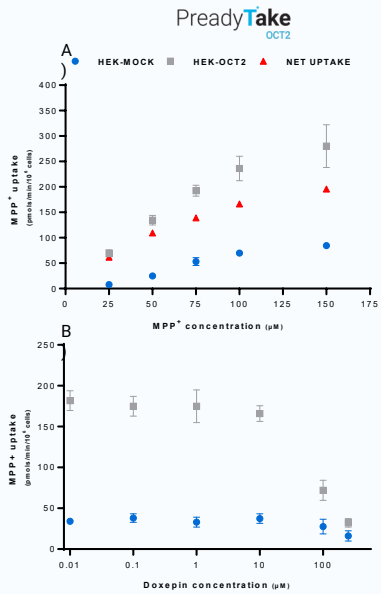


Figure 3. OCT2-mediated MPP+ internalization in the absence (Panel A) or presence (Panel B) of doxepin, an OCT2 inhibitor.

Data indicate that PreadyTake are compliant and useful *in vitro* tools to screen OATP1B3, OCT2 and MATE1-mediated drug-transporter interactions and/or induced drug hepatic/renal toxicity at the early stages of drug development.

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REFERENCES:

- *Transporter-Mediated Drug Interactions Guidance for Industry, 2020. Food and Drug Administration (FDA). In Vitro Drug Interaction Studies — Cytochrome P450 Enzyme- and Interactions Guidance for Industry. U.S.*
- *Nies AT et al, Arch Toxicol 90:1555–1584, 2016.*
- *Tweedie et al, Clinical Pharmacology & Therapeutics, 94(1), 113-125, 2013.*
- *Hermann Koepsell et al, Pharm Research, 24:1227-1251, 2007.*