SUPPLEMENTARY INFORMATION

Prediction of Transporter-Mediated Rosuvastatin Hepatic Uptake Clearance and Drug Interaction in Humans Using Proteomics-Informed REF Approach

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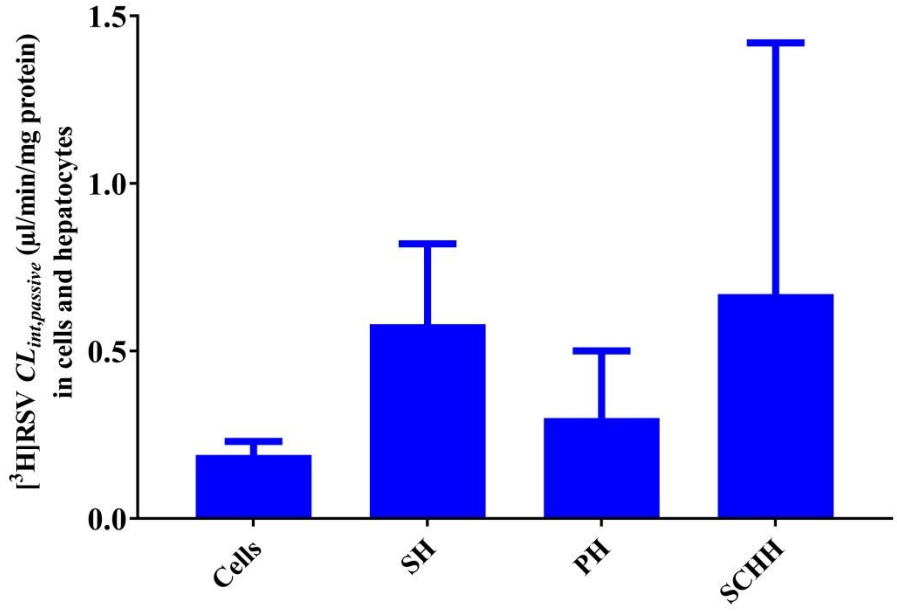
Supplementary Fig. 1. [^{3}H]RSV $CL_{int,passive}$ in transporter-expressing cells and hepatocyte models was not significantly different (Tukey's multiple comparisons test). Data for hepatocyte models are mean±SD (n=4), each conducted in triplicate. Data for the transporter-expressing cells are mean±SD of data obtained in CHO, MDCKII and HEK293 cells, each conducted in triplicate.

Supplementary Fig. 2. IVIVE of RSV hepatic $CL_{uptake,\ in\ vivo}$ adjusted for the protein-mediated uptake of RSV in transporter-expressing cells assuming sinusoidal uptake CL is the RDS. The transporter-expressing cells predicted the *in vivo* hepatic CL within 2-fold of the observed value (850.5 ml/min). The solid and dashed lines show the 95% CI of the observed hepatic CL and 2-fold lower limit of the mean observed hepatic CL (425 ml/min). When the transporter-mediated $CL_{int,uptake,cells}$ was adjusted for the increase in the RSV uptake in the presence of 100% HP or 5%HSA , the transporter-expressing cells successfully predicted hepatic $CL_{uptake,\ in\ vivo}$ (480 ml/min with 100% HP; 520 ml/min in 5%HSA) if assuming sinusoidal uptake CL is the RDS.

Supplementary Fig. 1.



Supplementary Fig. 2.