

Additional Data file 2:

Table S2. Substrate drugs with different affinities for either ABCB1 and/or ABCG2 were selected based on literature data. Similarly, their potencies to inhibit these transporters were also taken from literature reports. In all case, the concentrations used in the accumulation studies were far below the IC₅₀ for either transporter.

Affinity of substrates for transport by ABCB1 and ABCG2					Potency to inhibit ABCB1 and ABCG2			
Reported substrate affinity	Substrate drug	Affinity ABCB1	Affinity ABCG2	Reference	Cell line overexpressing ABCB1/ABCG2	IC ₅₀ ABCB1 (μM)	IC ₅₀ ABCG2 (μM)	Reference
P-gp only substrate	Loperamide	+	-	[1]	-	NR	NR	-
	Verapamil	+	-	[2]	MDCK-MDR1 MDCK-BCRP	6.9	137.8	[3]
Moderate dual substrate	Ibrutinib	+	+	[4]	KB-C2 K562/AO2 HEK393-ABCB1	1.0 >2.5 >2.5	NR	[5]
	Erlotinib	+	+	[6]	KB-C2 HEK293-ABCG2	10	2.5	[6]
	Palbociclib	+	+	[7]	KB-C2	3	NR	[8]
	Dasatinib	+	+	[9]	HEK293-ABCB1 HEK293-ABCG2	>10	>10	[10]
Strong dual substrate	Vemurafenib	+	+	[11]	HEK293-ABCB1 H460/MX-20 HEK293MDR19 MCF7-FLV1000 MCF7-AdVp3000 S1-M1-80	>20 >50	>20 1.24 4.91 2.60	[12, 13]
	Afatinib	+	+	[14]	A2780T H460/MX20 HEK293-ABCG2	2	>1 0.5	[15, 16]

NR= not reported

Supplemental references to Table S2

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Figure S2. **Accumulation of drugs in MDCKII parent, MDCK-MDR1 and MDCK-BCRP cells** We used an 8-drug mixture (loperamide, verapamil, erlotinib, vemurafenib, palbociclib, ibrutinib, dasatinib and afatinib), each at 100 nM, in combination with increasing concentrations of elacridar or tariquidar. Nonlinear curves were fitted using Graphpad. Unsuccessful fitting (no line) indicates that the compound is not transported by the respective ABC transporter. The drugs are classified as: (I) Abcb1 only substrates, (II) Abcb1 and weak Abcg2 substrates and (III) Abcb1 and strong Abcg2 substrates, as shown below. The inhibitor concentration vs intracellular drug level concentrations were fitted using the [Agonist] vs response –Variable slope (four parameters) nonlinear fit in Graphpad Prism 10.1.2. The dashed lines indicate the 90% CI.

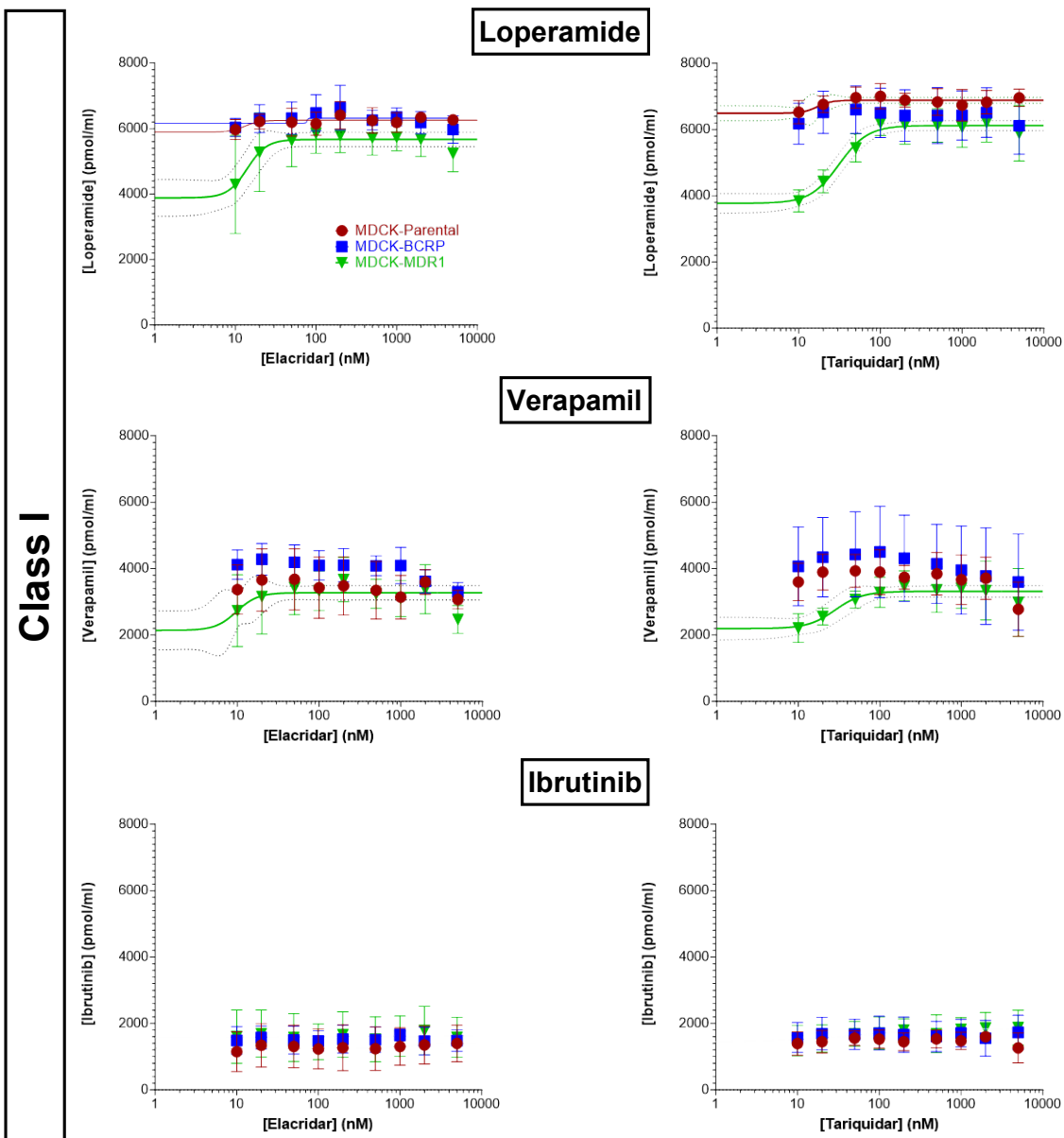
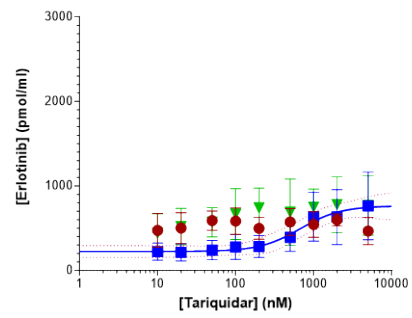
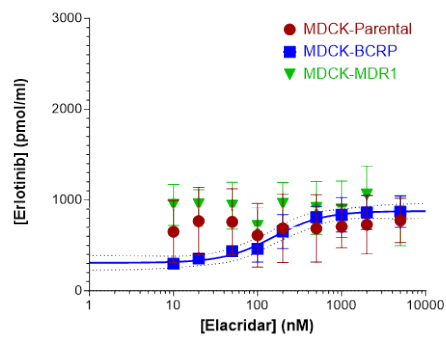


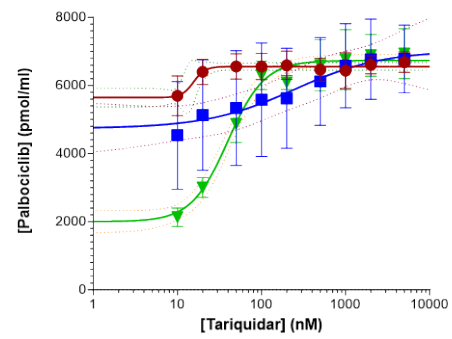
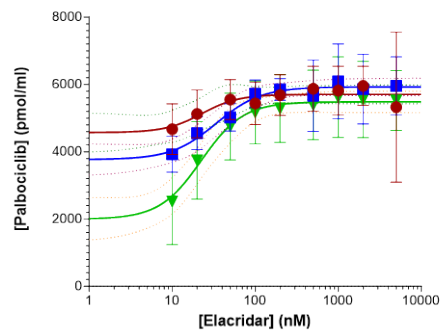
Figure S2 (continued)

Class II

Erlotinib



Palbociclib



Dasatinib

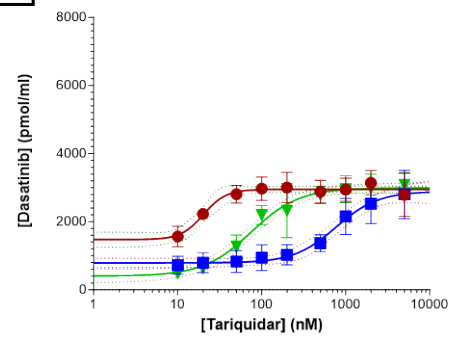
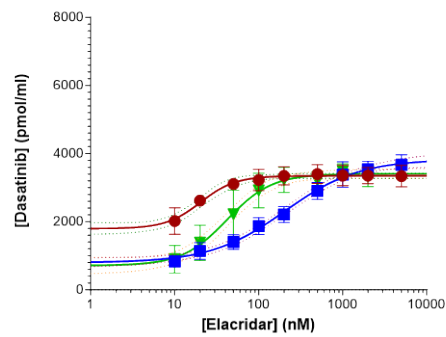


Figure 2 (continued)

