SUPPLEMENTAL FILE 2

***In Vitro* IC_{50} (µM) Values for Drugs**

Drug		Overall	Cell Line			Calculation Method		
			Caco-2	LLC-PK1-MDR1	MDCK-MDR1	ER	NSF	$P_{app,BL-AP}$
Amiodarone	Count	21	6	9	6	6	10	5
	Geometric Mean	11.42	5.90	13.36	17.45	7.78	13.05	13.83
	Minimum	4	4	5.48	8.7	4	5.48	4.4
	Maximum	45.6	12.3	45.6	42.4	12.3	45.6	20.9
Atorvastatin	Count	3	2	1	0	1	2	0
	Geometric Mean	39.80	64.62	15.1	-----	43.5	38.07	-----
	Minimum	15.1	43.5	15.1	-----	43.5	15.10	-----
	Maximum	96	96	15.1	-----	43.5	96	-----
Bepridil	Count	4	0	3	1	1	1	2
	Geometric Mean	12.11	-----	11.62	13.7	3.8	10.6	23.11
	Minimum	3.8	-----	3.8	13.7	3.8	10.6	13.7
	Maximum	39	-----	39	13.7	3.8	10.6	39
Carvedilol	Count	45	24	13	8	12	18	15
	Geometric Mean	3.45	2.55	4.72	5.10	1.56	4.96	4.22
	Minimum	0.15	0.16	0.15	2	0.15	0.16	0.6
	Maximum	40.6	40.6	32	10	25	32	40.6
Clarithromycin	Count	7	5	2	0	4	2	1
	Geometric Mean	20.41	16.14	36.74	-----	23.81	16.45	17
	Minimum	4.1	4.1	34	-----	7	4.1	17
	Maximum	66	66	39.7	-----	39.7	66	17
Conivaptan	Count	5	3	2	0	2	2	1
	Geometric Mean	23.99	33.63	14.46	-----	20.37	39.00	12.6
	Minimum	12.6	25	12.6	-----	16.6	39	12.6

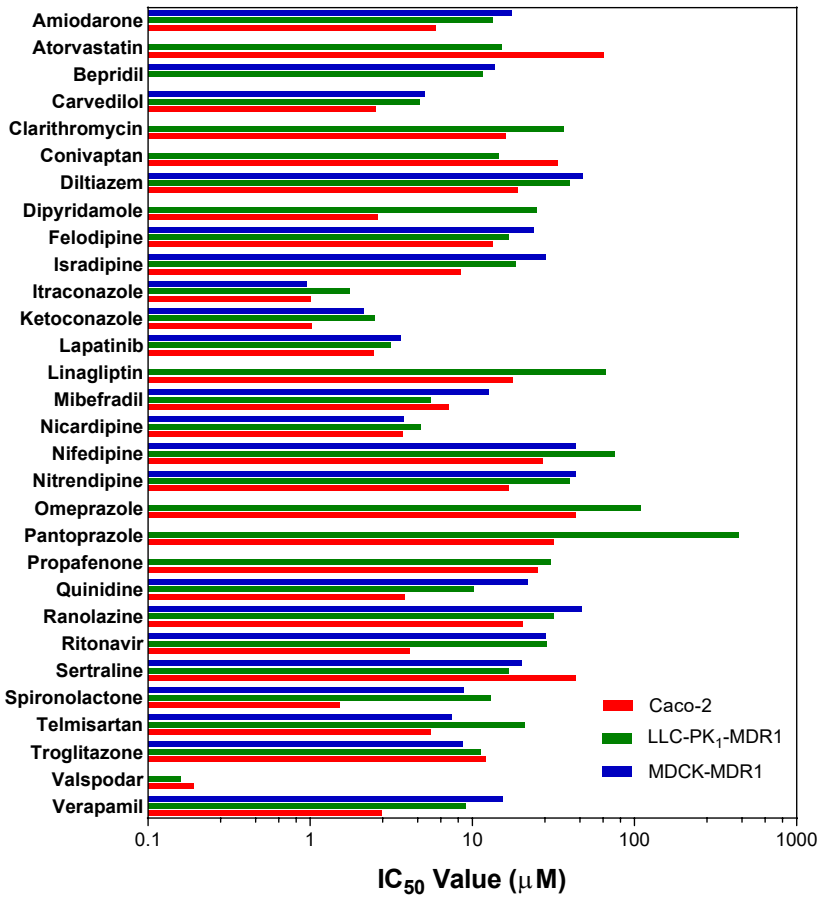
	Maximum	39	39	16.6	-----	25	39	12.6
Diltiazem	Count	40	23	7	10	10	18	12
	Geometric Mean	27.32	19.15	39.61	47.75	8.71	45.83	32.61
	Minimum	4.3	4.3	4.6	7.0	4.3	7.2	6.9
	Maximum	300	86.3	300	185.8	31.6	300	109.6
Dipyridamole	Count	8	3	5	0	2	2	4
	Geometric Mean	10.70	2.60	24.99	-----	14.44	7.75	10.83
	Minimum	1.5	1.5	9.7	-----	9.7	1.5	2.4
	Maximum	41	4.9	41	-----	21.5	40	41
Felodipine	Count	34	18	8	8	8	15	11
	Geometric Mean	16.13	13.35	16.70	23.80	5.76	21.22	23.44
	Minimum	0.9	0.9	4.22	6.6	0.9	4.4	2.7
	Maximum	85.8	68.1	63	85.8	39.8	63	85.8
Isradipine	Count	34	19	6	9	8	15	11
	Geometric Mean	13.38	8.46	18.43	28.39	6.62	18.33	14.51
	Minimum	2.9	2.9	7.7	7.2	2.9	6.6	5
	Maximum	54.5	21.4	40.2	54.5	13	53.9	54.5
Itraconazole	Count	12	7	4	1	5	2	5
	Geometric Mean	1.21	1.01	1.76	0.95	0.88	2.19	1.31
	Minimum	0.408	0.408	0.45	0.95	0.45	0.797	0.408
	Maximum	6.3	6	6.3	0.95	2	6	6.3
Ketoconazole	Count	20	12	4	4	6	6	8
	Geometric Mean	1.42	1.02	2.50	2.13	1.07	1.21	1.97
	Minimum	0.1	0.1	1.2	1.34	0.42	0.1	0.99
	Maximum	6.4	4.6	6.4	3.07	1.89	4.6	6.4
Lapatinib	Count	4	1	2	1	2	0	2
	Geometric Mean	3.06	2.47	3.15	3.6	1.92	-----	4.87
	Minimum	1.5	2.47	1.5	3.6	1.5	-----	3.6
	Maximum	6.6	2.47	6.6	3.6	2.47	-----	6.6
Linagliptin	Count	3	2	1	0	2	0	1

	Geometric Mean	27.36	17.61	66	-----	24.91	-----	33
	Minimum	9.4	9.4	66	-----	9.4	-----	33
	Maximum	66	33	66	-----	66	-----	33
Mibefradil	Count	39	24	7	8	8	18	13
	Geometric Mean	7.71	7.20	5.56	12.60	4.98	7.96	9.64
	Minimum	0.9	0.9	1.7	5.2	1.7	0.9	1.2
	Maximum	57.7	57.7	15.1	32.4	20.1	51.2	57.7
Nicardipine	Count	40	18	9	13	9	19	12
	Geometric Mean	3.95	3.71	4.82	3.76	1.54	6.49	3.65
	Minimum	0.1	0.1	1.1	0.8	0.1	0.9	0.8
	Maximum	45.7	24	45.7	11	6.3	45.7	21.4
Nifedipine	Count	30	20	4	6	10	13	7
	Geometric Mean	34.06	27.01	75.76	43.32	14.85	56.86	43.06
	Minimum	1.4	1.4	23	7.5	1.4	7.2	7.1
	Maximum	472	85.7	472	126	57.8	472	126
Nitrendipine	Count	33	25	4	4	10	14	9
	Geometric Mean	20.77	16.63	40.00	43.32	10.37	30.75	24.41
	Minimum	1.5	1.5	18.2	11.2	1.5	6.7	6.1
	Maximum	241.6	241.6	68.2	112.2	47	164.7	241.6
Omeprazole	Count	5	4	1	0	2	2	1
	Geometric Mean	52.35	43.48	110	-----	45.72	38.79	125
	Minimum	17.7	17.7	110	-----	19	17.7	125
	Maximum	125	125	110	-----	110	85	125
Pantoprazole	Count	3	2	1	0	2	1	0
	Geometric Mean	76.02	31.63	439	-----	156.65	17.9	-----
	Minimum	17.9	17.9	439	-----	55.9	17.9	-----
	Maximum	439	55.9	439	-----	439	17.9	-----
Propafenone	Count	4	2	2	0	1	3	0
	Geometric Mean	27.78	25.42	30.36	-----	20.3	30.84	-----
	Minimum	6.8	6.8	20.3	-----	20.3	6.8	-----

	Maximum	95	95	45.4	-----	20.3	95	-----
Quinidine	Count	66	40	13	14	19	23	24
	Geometric Mean	6.58	3.80	10.22	21.75	2.78	12.36	7.13
	Minimum	0.1	0.1	1	1.6	0.13	0.1	0.16
	Maximum	78.2	39.1	56	78.2	43.4	78.2	73
Ranolazine	Count	34	19	6	9	9	14	11
	Geometric Mean	27.57	20.48	31.63	47.17	11.26	48.27	28.15
	Minimum	3.5	3.8	10.7	3.5	3.5	11.7	9
	Maximum	198.8	83.2	130	198.8	35.5	198.8	100
Ritonavir	Count	10	6	3	1	3	4	3
	Geometric Mean	8.92	4.12	28.52	28.2	5.43	7.14	19.73
	Minimum	1.5	1.5	18	28.2	1.5	3.8	4.5
	Maximum	60.5	10	60.5	28.2	21.3	18	60.5
Sertraline	Count	16	10	4	2	3	8	5
	Geometric Mean	31.17	43.67	16.63	20.28	21.59	35.44	31.64
	Minimum	4.6	18.5	4.6	19.4	12.9	4.6	18.5
	Maximum	92	92	56	21.2	33.9	92	56
Spironolactone	Count	6	3	2	1	2	1	3
	Geometric Mean	4.17	1.52	12.94	8.8	1.59	2.84	8.99
	Minimum	0.377	0.377	6.7	8.8	0.377	2.84	3.308
	Maximum	25	3.308	25	8.8	6.7	2.84	25
Telmisartan	Count	42	28	8	6	12	16	14
	Geometric Mean	7.44	5.54	20.99	7.42	5.27	8.77	8.29
	Minimum	1.2	1.2	12.2	2.1	2	1.6	1.2
	Maximum	40.7	31	40.7	20.7	20.7	31	40.7
Troglitazone	Count	36	28	3	5	11	15	10
	Geometric Mean	11.43	12.01	11.22	8.77	7.39	15.96	11.19
	Minimum	2	2	7.4	6	2	6	4.9
	Maximum	53.7	53.7	15.9	11.4	21.2	53.7	26.9
Valspodar	Count	8	5	3	0	1	3	4

	Geometric Mean	0.18	0.19	0.16	-----	0.38	0.29	0.10
	Minimum	0.0222	0.09	0.02	-----	0.38	0.11	0.0222
	Maximum	2.1	2.1	0.48	-----	0.38	2.1	0.48
Verapamil	Count	79	52	12	15	22	27	30
	Geometric Mean	4.59	2.77	9.15	15.30	1.62	8.30	5.77
	Minimum	0.063	0.063	0.57	1.7	0.063	0.7	0.17
	Maximum	224	48.3	224	44	26	57	224

Overall = all IC_{50} data regardless of cell line or calculation method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Bepridil
Carvedilol
Clarithromycin
Conivaptan
Diltiazem
Dipyridamole
Felodipine
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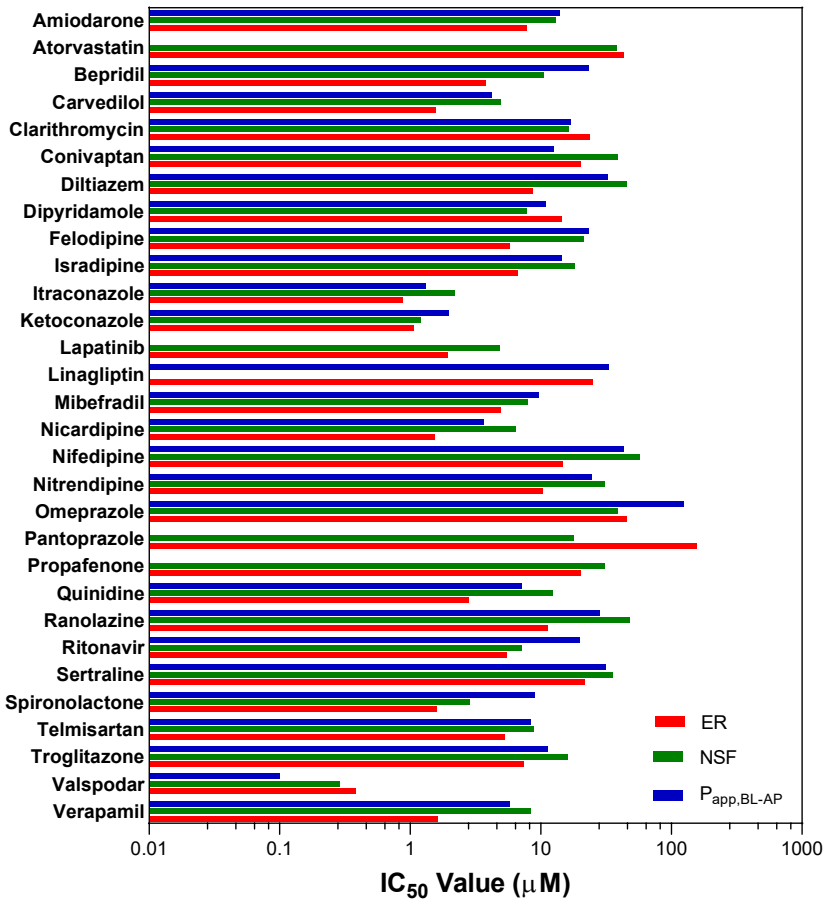
Itraconazole
Ketoconazole
Lapatinib
Linagliptin
Mibefradil
Nicardipine
Nifedipine
Nitrendipine
Omeprazole
Pantoprazole
Propafenone
Quinidine
Ranolazine
Ritonavir
Sertraline
Spironolactone
Telmisartan
Troglitazone
Valspodar
Verapamil
Caco-2
LLC-PK1-MDR1
MDCK-MDR1
0.1
1
10
100
1000
IC50 Value (μM)


Amiodarone
Atorvastatin
Bepridil
Carvedilol
Clarithromycin
Conivaptan
Diltiazem
Dipyridamole
Felodipine
Isradipine
Itraconazole
Ketoconazole
Lapatinib
Linagliptin
Mibefradil
Nicardipine
Nifedipine
Nitrendipine
Omeprazole
Pantoprazole
Propafenone
Quinidine
Ranolazine
Ritonavir
Sertraline
Spironolactone
Telmisartan
Troglitazone
Valspodar
Verapamil
ER
NSF
Papp,BL-AP
0.01
0.1
1
10
100
1000
IC50 Value (μM)

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