Supplementary information

Impact of V9302, a competitive antagonist of transmembrane glutamine flux on resistance reversal in breast cancer cell lines

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Table S1. Interactions of V9302 with doxorubicin and cisplatin on breast cancer cell lines (HTB-26, T47D, KCR, MCF-7).

Cell lines	Compounds	Starting concentration of V9302 (μM)	Ratio	Combination index	SD ±	Type of interaction
MDA-MB-231	V9302+CIS	90	0.9:1	0.871	0.06	slight synergism
			1.8:1	0.722	0.17	moderate synergism
			3.6:1	1.272	0.42	moderate antagonism
			7.2:1	103.686	28.89	very strong antagonism
			14.4:1	84.075	31.77	very strong antagonism
			28.8:1	142.592	28.77	very strong antagonism
	V9302+DOX	90	10.44:1	1.231	0.34	moderate antagonism
			20.88:1	0.819	0.014	moderate synergism
			41.76:1	0.747	0.14	moderate synergism
			83.52:1	0.828	0.53	moderate synergism
			167.05:1	0.133	0.02	strong synergism
T-47D	V9302+CIS	80	0.8:1	0.579	0.06	synergism
			1.6:1	0.872	0.17	slight synergism
			3.2:1	0.664	0.12	synergism
			6.4:1	0.785	0.07	moderate synergism
			12.8:1	35.675	15.28	very strong antagonism
			25.6:1	10.901	4.08	very strong antagonism
	V9302+DOX	80	9.28:1	1.202	0.11	moderate antagonism
			18.56:1	61.619	23.83	very strong antagonism
			37.12:1	0.732	0.11	moderate synergism
			74.24:1	1.157	0.21	slight antagonism
			148.48:1	22.130	5.53	very strong antagonism
			296.96:1	17.848	7.16	very strong antagonism
KCR	V9302+CIS	100	1:01	58.030	8.21	very strong antagonism
			2:01	0.967	0.06	additive effect
			4:01	0.886	0.02	slight synergism
			8:01	0.787	0.03	moderate synergism
			16:01	1.551	0.27	antagonism
			32:1.00	0.884	2.21	slight synergism
MCF-7	V9302+CIS	10.92	0.11:1	1.46	0.18	antagonism
			0.22:1	1.515	0.188	antagonism
			0.44:1	1.667	0.17	antagonism
			0.87:1	1.742	0.25	antagonism
			1.75:1	1.741	0.36	antagonism
			3.5:1	1.608	0.3	antagonism
	V9302+DOX	10.92	1.27:1	0.314	0.37	synergism
			2.54:1	0.884	0.19	slight synergism
			5.067:1	0.84	0.12	moderate synergism
			10.13:1	0.672	0.09	synergism
			20.27:1	0.864	0.1	moderate synergism
			40.54:1	1.257	0.19	moderate antagonism

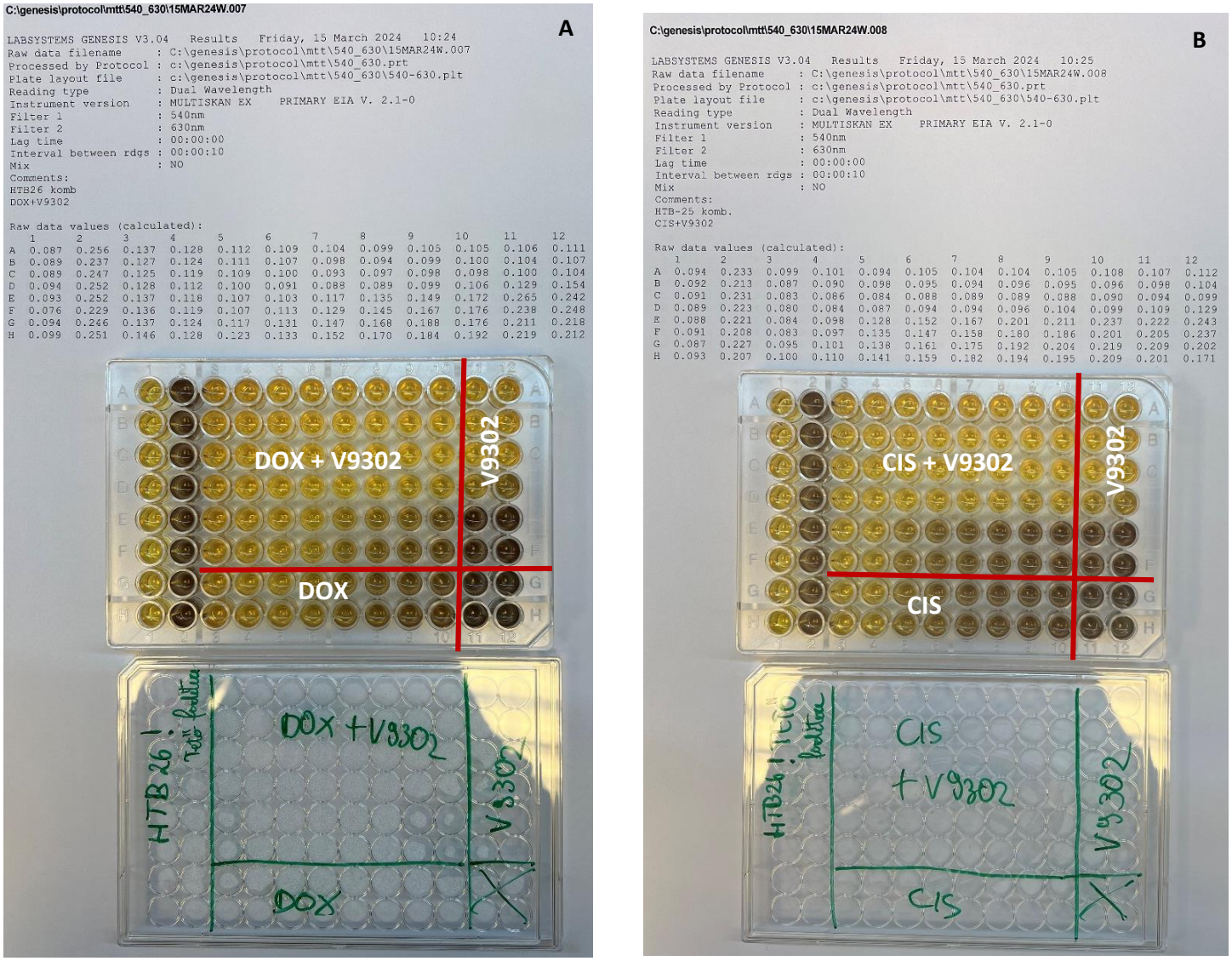


Figure S1A: Photo of the combination plate of doxorubicin and V9302 on MDA-MB-231 cells. **B:** Photo of the combination plate of cisplatin and V9302 on MDA-MB-231.

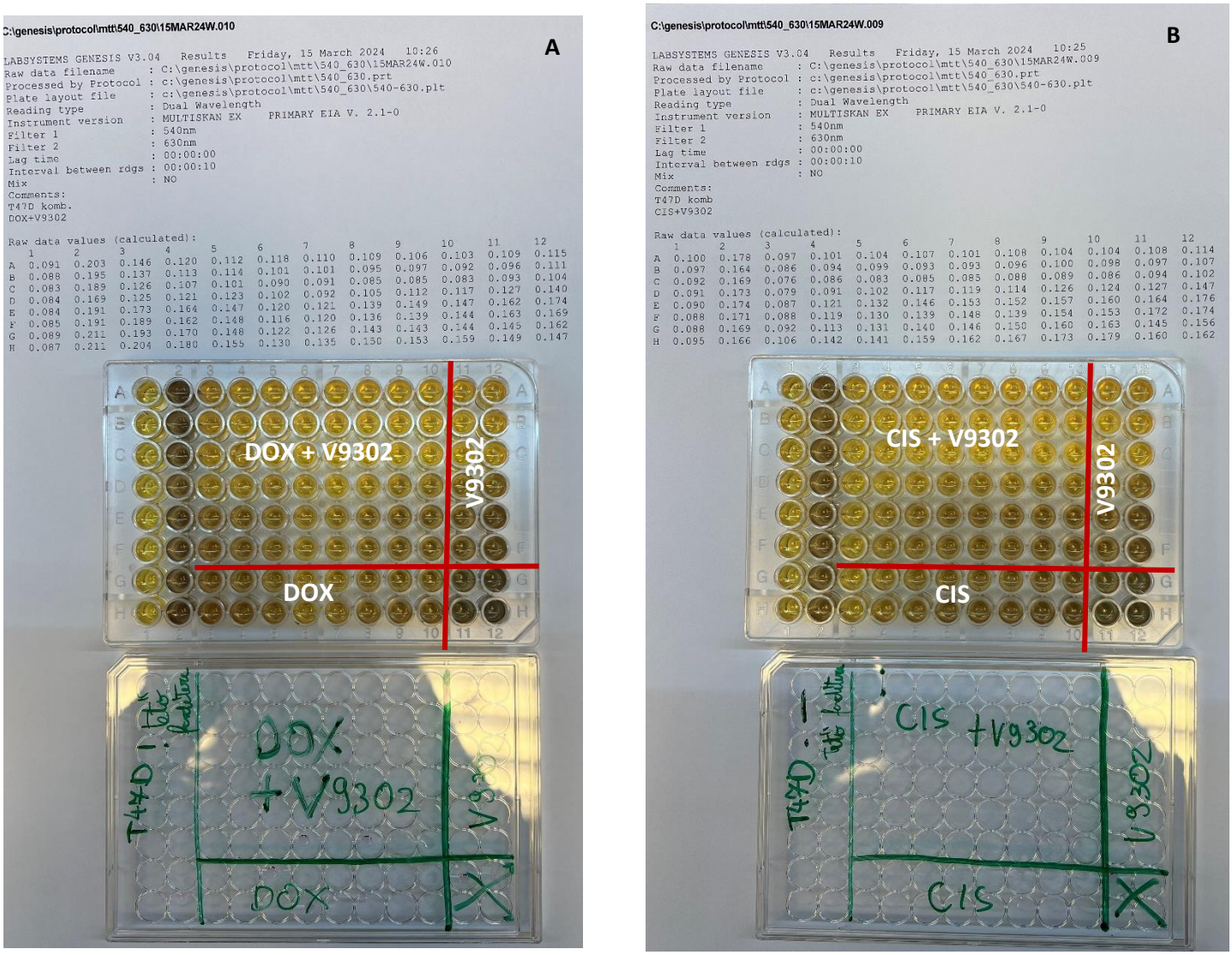
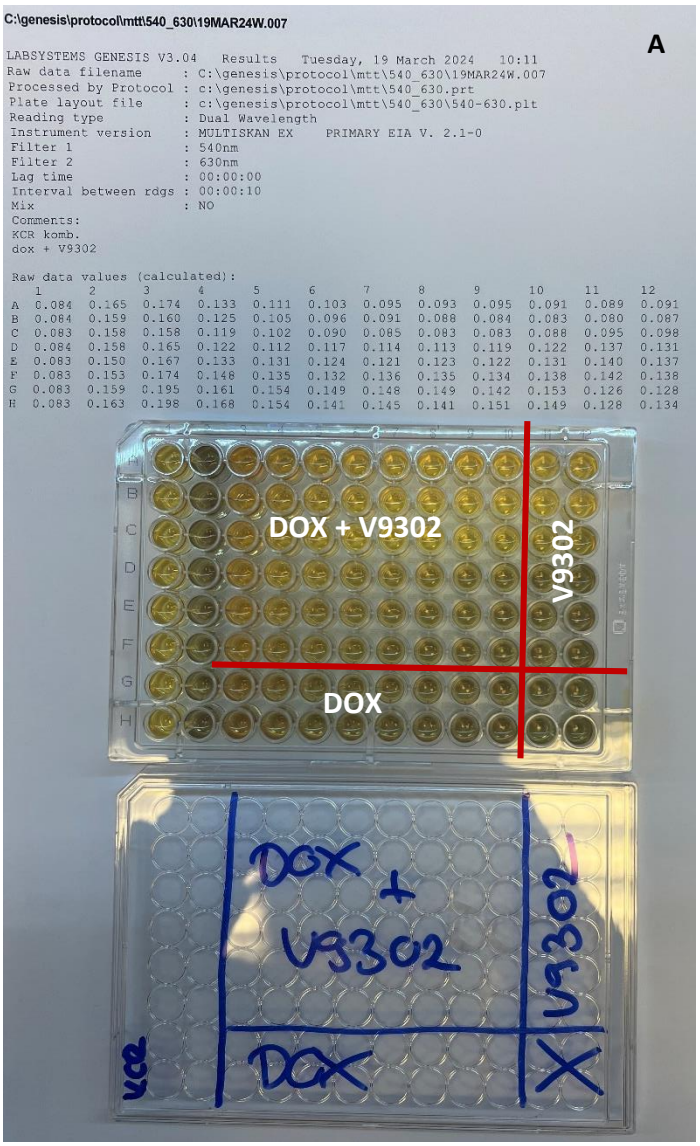


Figure S2A: Photo of the combination plate of doxorubicin and V9302 on T47D cells. **B:** Photo of the combination plate of cisplatin and V9302 on T47D cells.



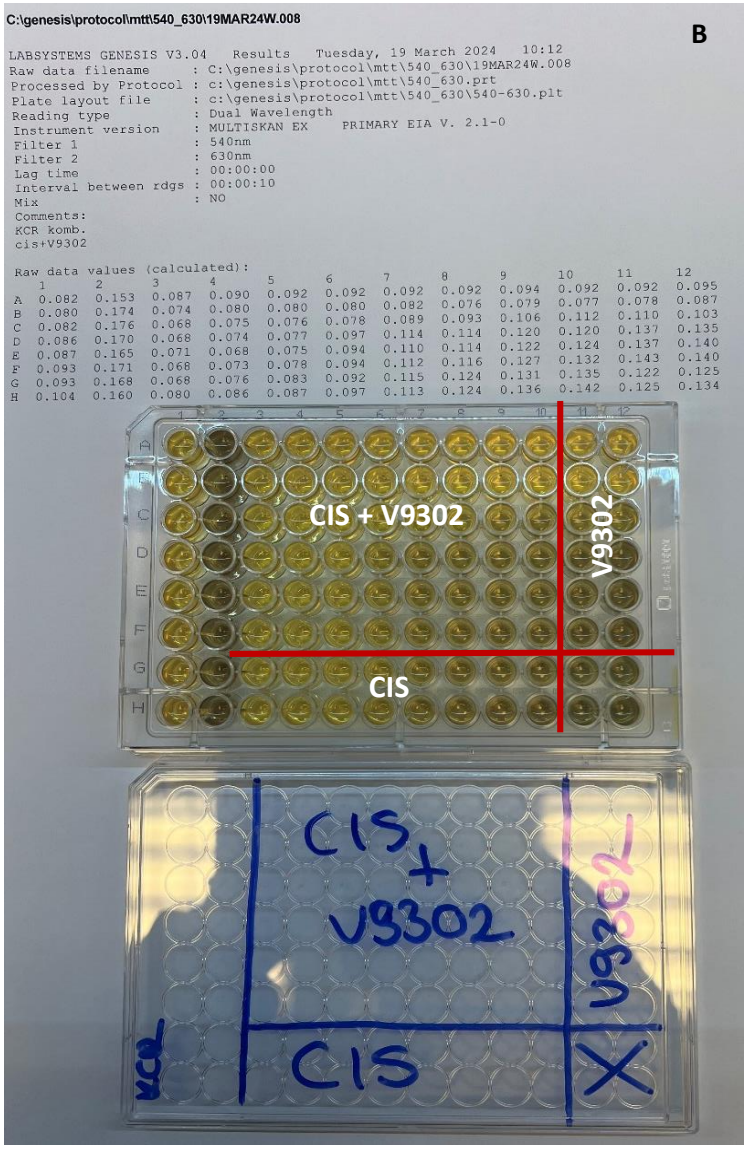


Figure S3A: Photo of the combination plate of doxorubicin and V9302 on KCR cells. **B:** Photo of the combination plate of cisplatin and V9302 on KCR cells.

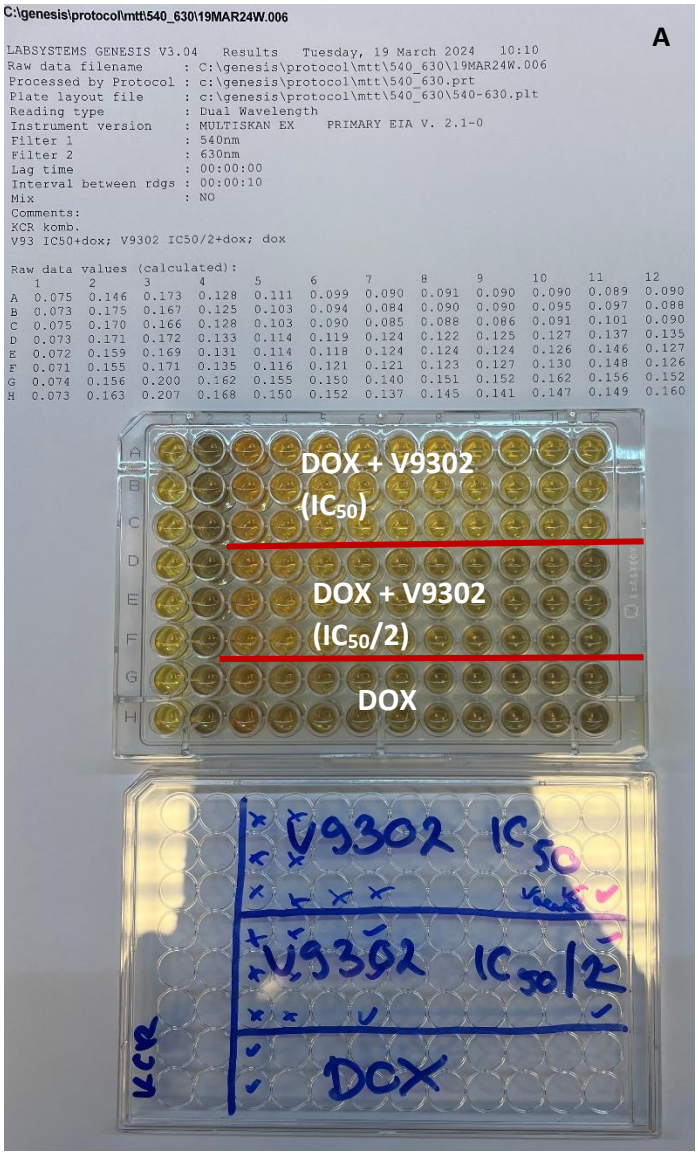


Figure S4A: Photo of the combination plate of doxorubicin and V9302 (at concentration IC_{50} and $IC_{50}/2$ on KCR cells.

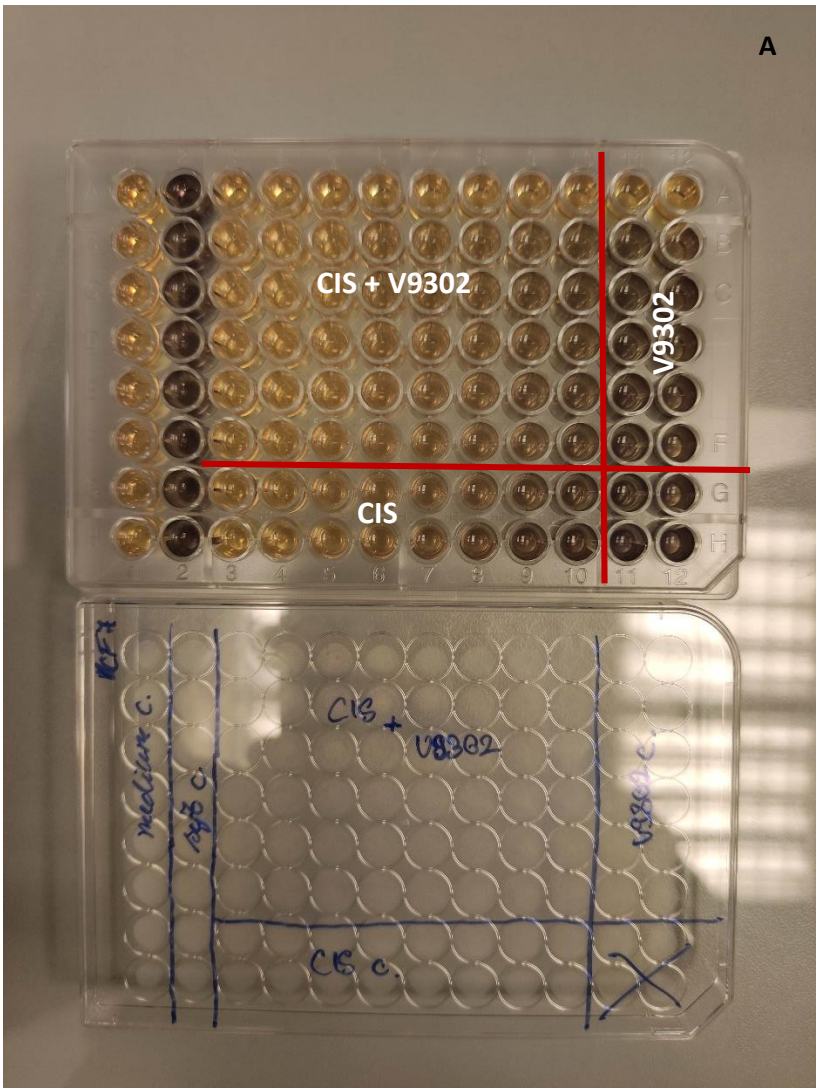


Figure S5A: Photo of the combination plate of cisplatin and on MCF-7 cells.

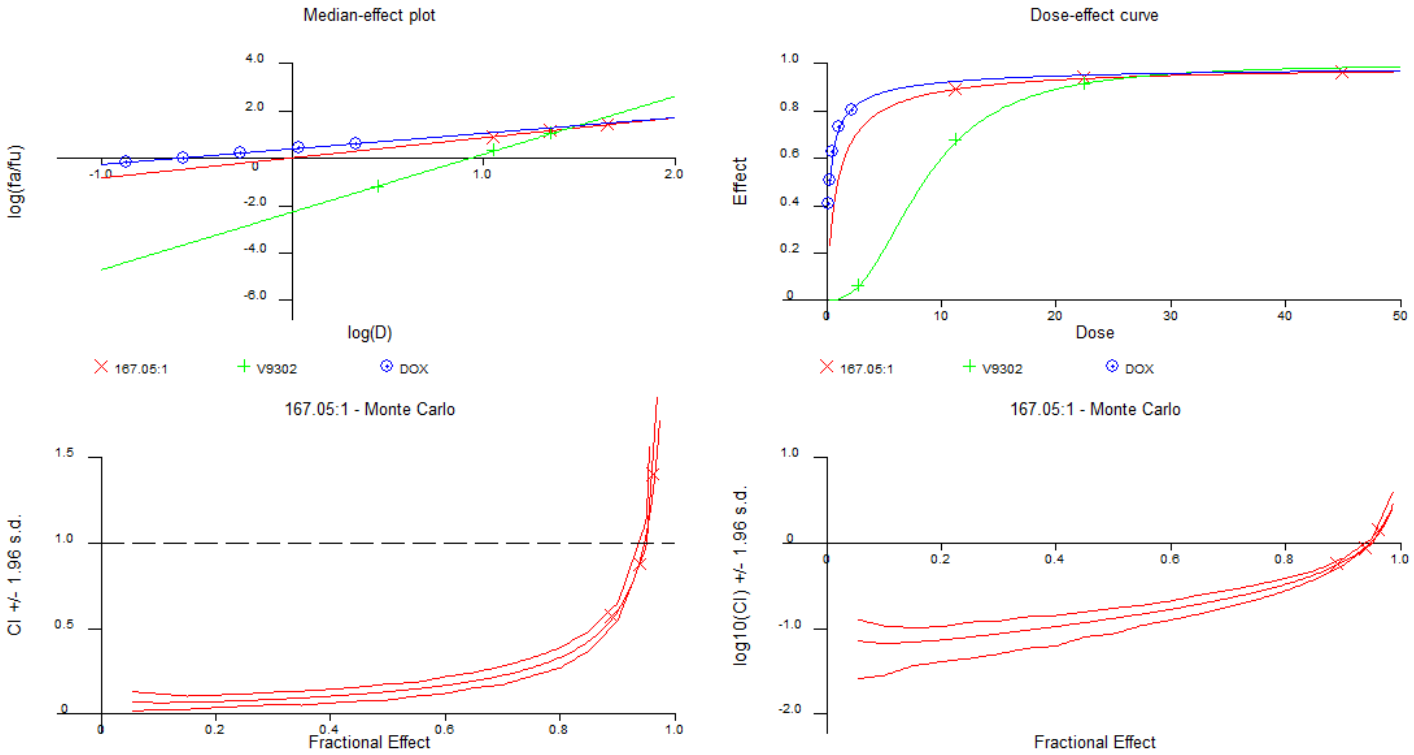


Figure S6. Graphs of checkerboard combination assay on MDA-MB-231 cells with doxorubicin and V9302 at ratio 167.05:1.

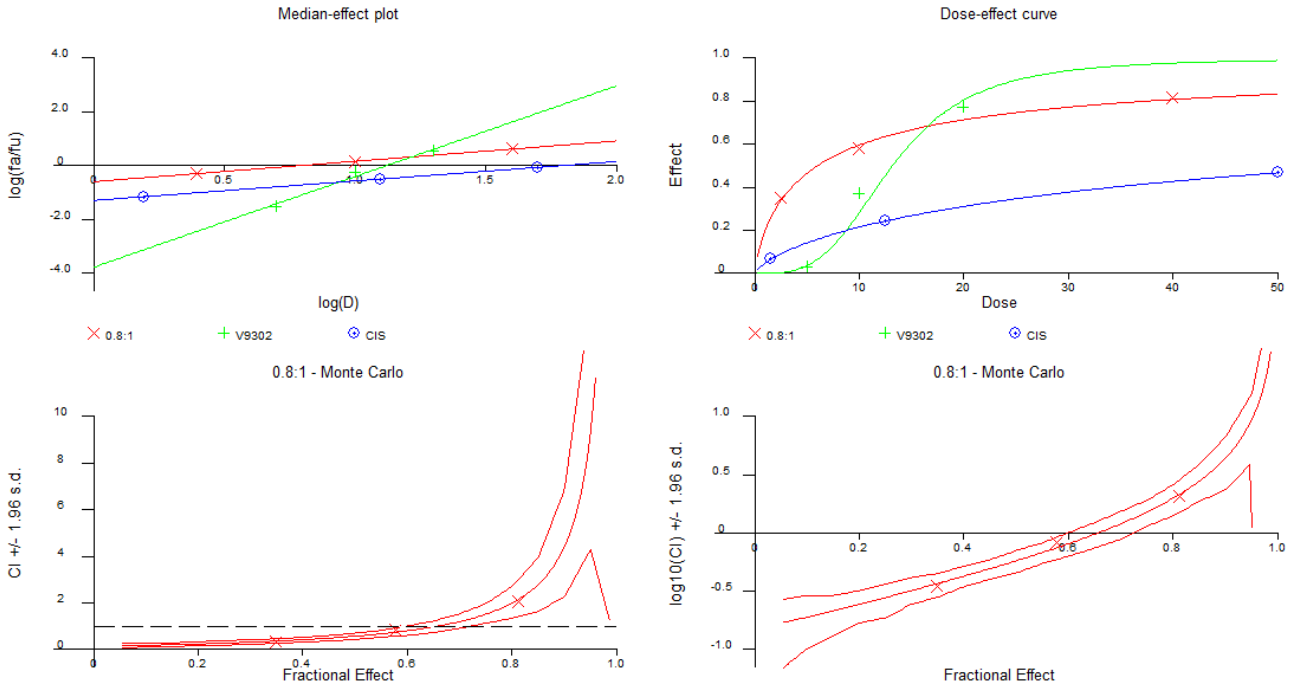


Figure S7. Graphs of checkerboard combination assay on MDA-MB-231 cells with cisplatin and V9302 at ratio 0.9:1.

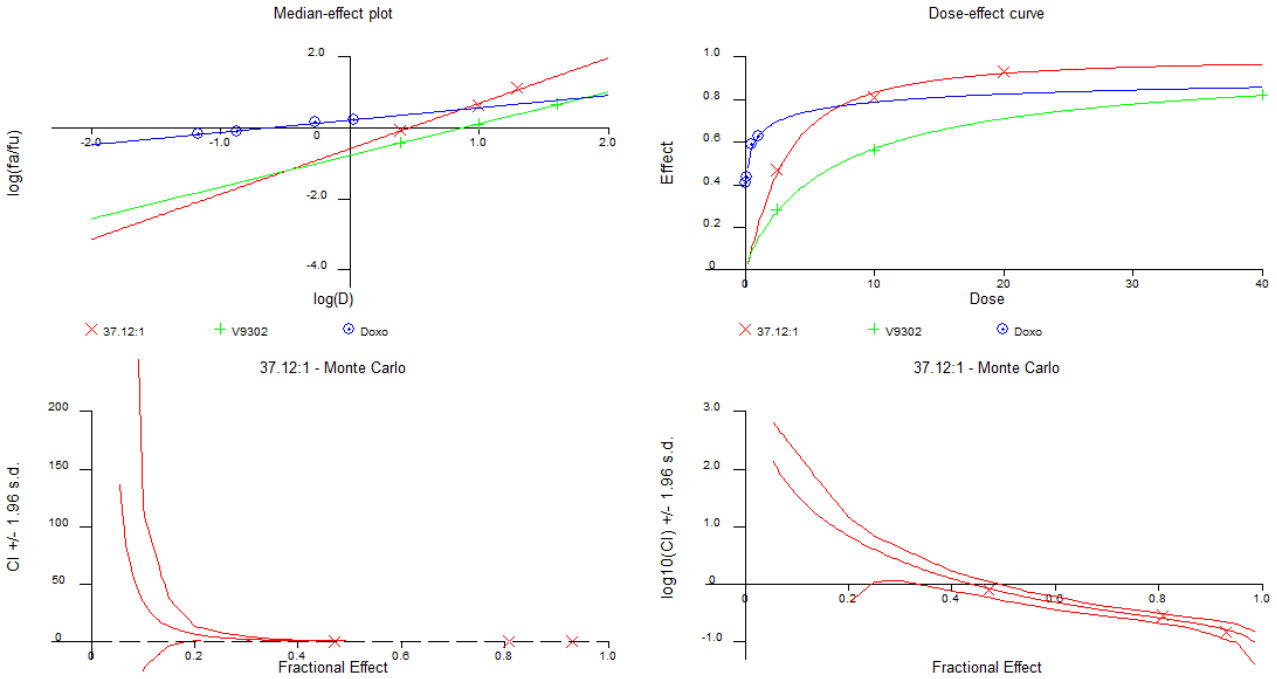


Figure S8. Graphs of checkerboard combination assay on T47D cells with doxorubicin and V9302 at ratio 37.12:1.

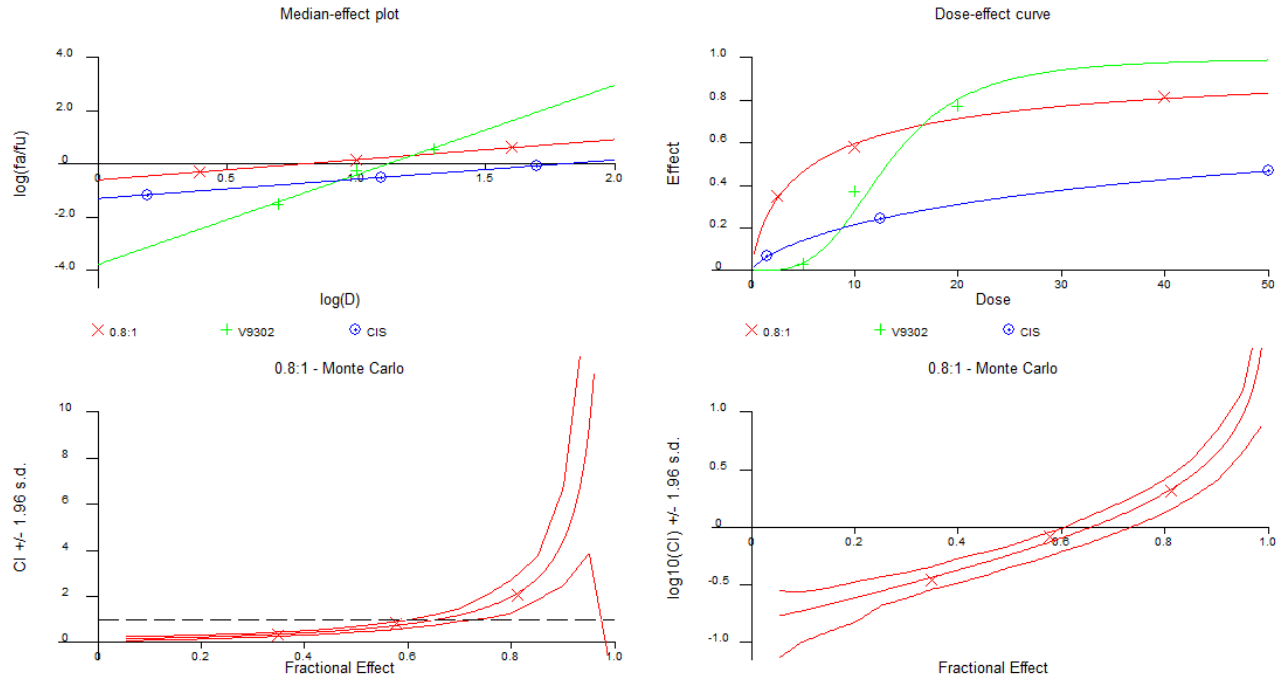


Figure S9. Graphs of checkerboard combination assay on T47D cells with cisplatin and V9302 at ratio 0.8:1.

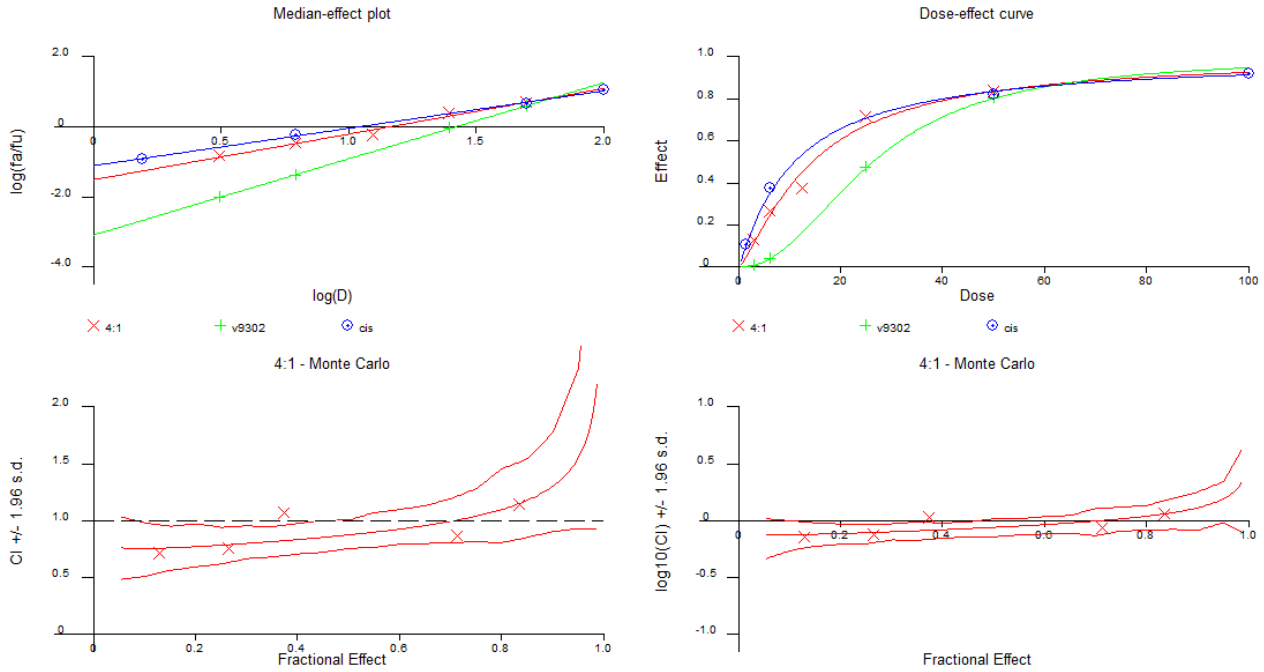


Figure S10. Graphs of checkerboard combination assay on KCR cells with cisplatin and V9302 at ratio 4:1.

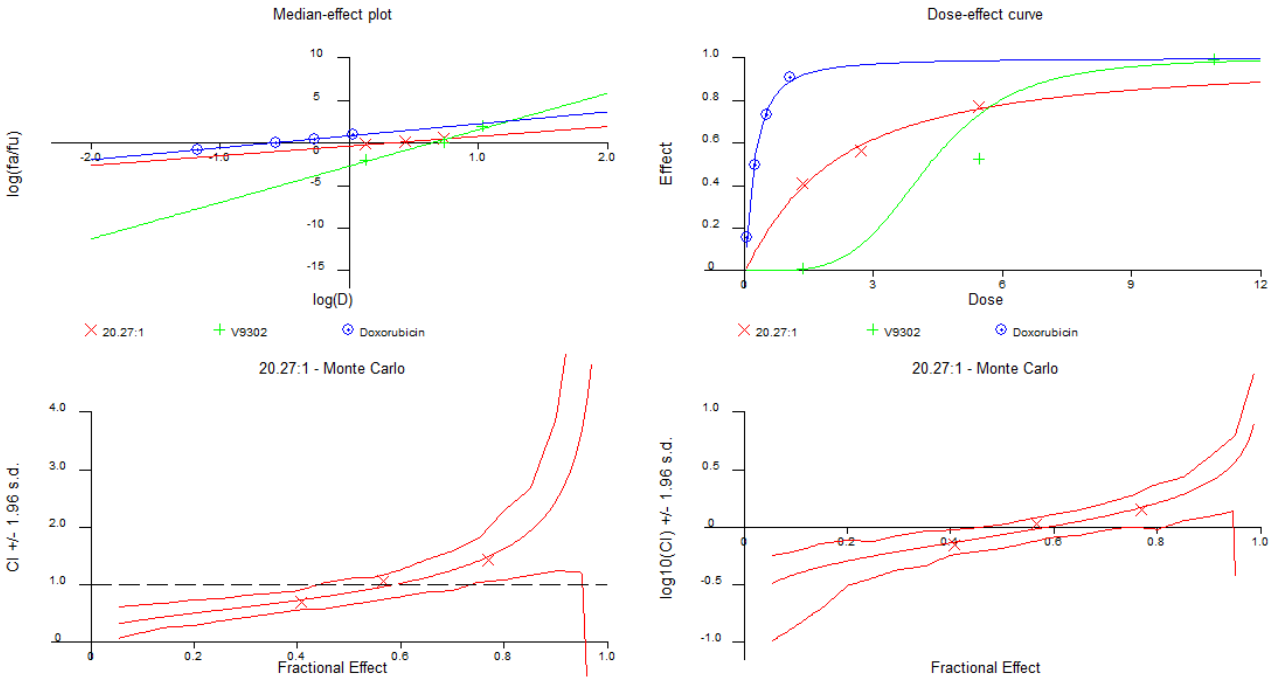


Figure S11. Graphs of checkerboard combination assay on MCF-7 cells with doxorubicin and V9302 at ratio 20.27:1.

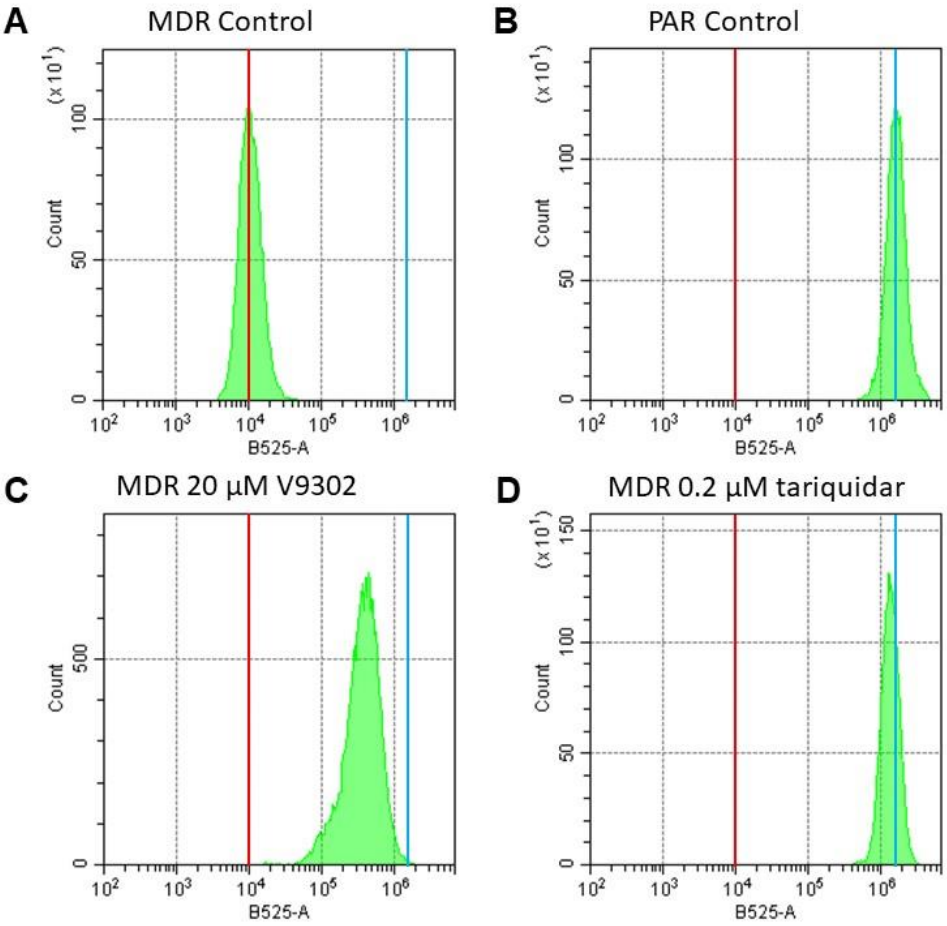


Figure S12. Rhodamine-123 accumulation by parental (PAR) L5178Y mouse T-lymphoma and its Pgp overexpressing counterpart (MDR). Tariquidar was used at 0.2 µM as a positive control on MDR cells, V9302 was applied at 20 µM on MDR cells.