

**Supplementary Table 1: ELDA Data From Figure 2C**

Group	Dose	Tested	Response
SW480c	1000	32	32
SW480c	100	32	32
SW480c	10	64	56
SW480c	1	86	23
SW480cldn1	1000	32	32
SW480cldn1	100	32	32
SW480cldn1	10	64	60
SW480cldn1	1	82	31

Group	Dose	Tested	Response
SW620c	1000	32	32
SW620c	100	32	32
SW620c	10	64	64
SW620c	1	87	39
SW620cldn1 KO	1000	32	32
SW620cldn1 KO	100	32	31
SW620cldn1 KO	10	64	56
SW620cldn1 KO	1	92	42

Group	Dose	Tested	Response
DLDC	1000	32	32
DLDC	100	32	32
DLDC	10	64	62
DLDC	1	86	39
DLDCldn1 KO	1000	32	32
DLDCldn1 KO	100	32	32
DLDCldn1 KO	10	64	61
DLDCldn1 KO	1	90	25

Confidence Intervals for 1/(tumor-initiating cell frequency)			
Group	Lower	Estimate	Upper
SW480c	5.99	4.73	3.76
SW480cldn1	4.27	3.36	2.67

Confidence Intervals for 1/(tumor-initiating cell frequency)			
Group	Lower	Estimate	Upper
SW620c	2.75	2.19	1.79
SW620cldn1 KO	6.24	4.93	3.93

Confidence Intervals for 1/(tumor-initiating cell frequency)			
Group	Lower	Estimate	Upper
DLDC	3.29	2.59	2.08
DLDCldn1 KO	4.68	3.70	2.96

**Supplementary Table 2: Data Point Statistics From Figure 3D**

Tumor Growth Measurements (mm<sup>3</sup>)

	620c Con			620c 5FU			620KO Con			620KO 5FU		
	Mean	SEM	N	Mean	SEM	N	Mean	SEM	N	Mean	SEM	N
Day 1	100.644	21.17167	6	50.51902	18.10961	7	44.416	9.789947	6	30.19214	15.04131	5
Day 3	217.367	26.21799	6	210.7758	77.69114	7	128.5179	36.1271	6	45.27264	21.46464	5
Day5	290.141	40.21773	6	277.0836	90.63381	7	186.5414	50.40482	6	130.134	84.2872	5
Day7	419.0218	48.5826	6	449.8146	148.8243	7	326.6267	53.38496	6	135.6436	89.11413	5
Day9	581.2568	64.65631	6	638.2379	238.6093	7	435.9135	80.20622	6	160.6901	109.1501	5
Day11	776.7296	97.3065	6	608.1942	252.0772	6	483.0484	114.2004	6	123.669	83.54091	5
Day 13	923.0774	160.6091	6	1030.179	408.4982	5	634.6148	136.2622	6	178.1978	104.3876	5
Day 15	1022.524	136.2686	6	1258.137	497.4778	5	858.1578	114.7692	6	229.3916	97.52323	5

Excised Tumor Volume (mm<sup>3</sup>)

	620c Con			620KO Con		
	Mean	SEM	N	Mean	SEM	N
Control	1128.272	226.5349	6	839.9263	173.8126	6
5FU	1081.395	442.2961	5	153.6975	58.00518	5

Excised Tumor Mass (g)

	620c Con			620KO Con		
	Mean	SEM	N	Mean	SEM	N
Control	0.617583	0.123521	6	0.4654	0.115897	6
5FU	0.69738	0.276032	5	0.14482	0.064403	5

**Supplementary Table 3: ELDA data from Figure 7C**

Group	Dose	Tested	Response
SW480cldn1	1000	32	32
SW480cldn1	100	32	32
SW480cldn1	10	64	60
SW480cldn1	1	86	24
SW480cldn1 EPH KO	1000	32	32
SW480cldn1 EPH KO	100	32	26
SW480cldn1 EPH KO	10	64	9
SW480cldn1 EPH KO	1	90	2

Confidence Intervals for 1/(tumor-initiating cell frequency)			
Group	Lower	Estimate	Upper
SW480cldn1	4.83	3.80	3.02
SW480cldn1 EPH KO	85.69	60.70	43.00