Supplementary Materials for

Basal expression of RAD51 foci predicts olaparib response in patient-derived ovarian cancer xenografts

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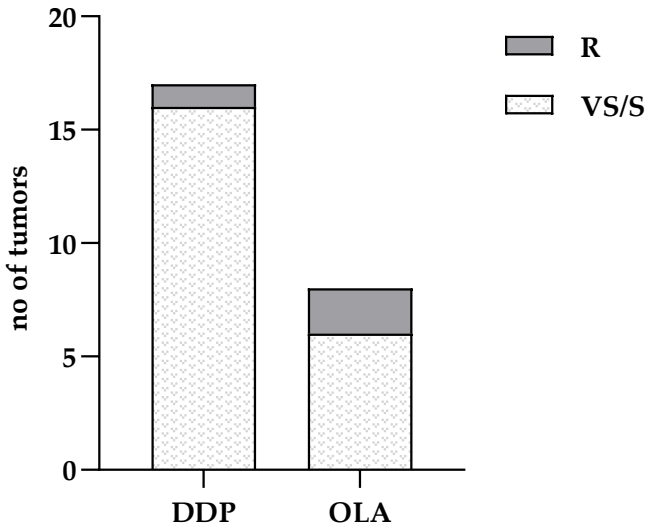


Figure S1. Distribution of the HR deficient (HRD) OC-PDXs based on their response to therapy

17 HRD OC-PDXs were divided into very sensitive and sensitive (VS/S) or resistant (R) to cisplatin (DDP) and olaparib (OLA).

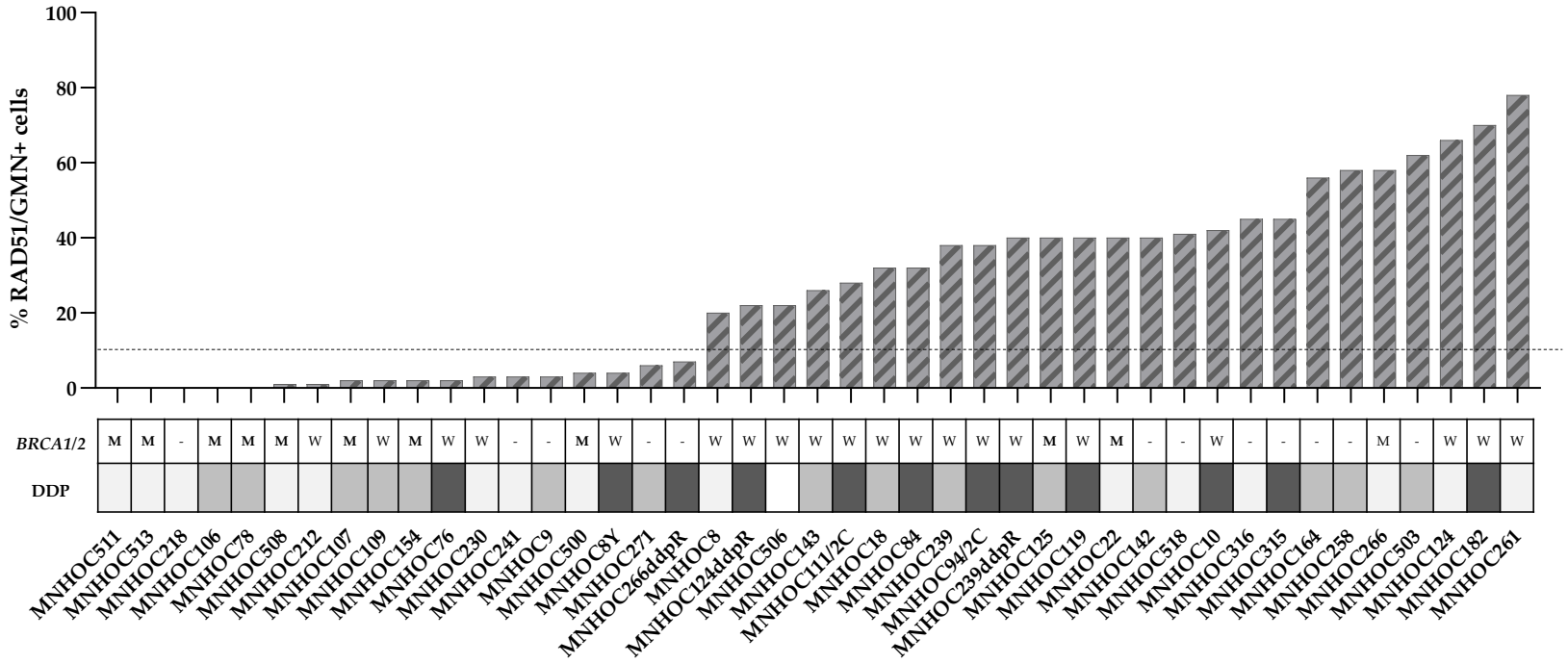
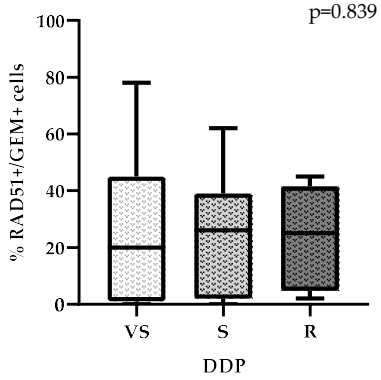


Figure S2. Percentages of cells positive to RAD51 foci in OC-PDXs and their responses to cisplatin

Each bar represents the percentage of cells in FFPE OC-PDX tumor samples. For each PDX the BRCA1/2 mutational status (M, mut; W, wild-type) is reported and sensitivity to cisplatin (DDP) (very sensitive, pale grey; sensitive, grey; resistant, dark grey squares).

A



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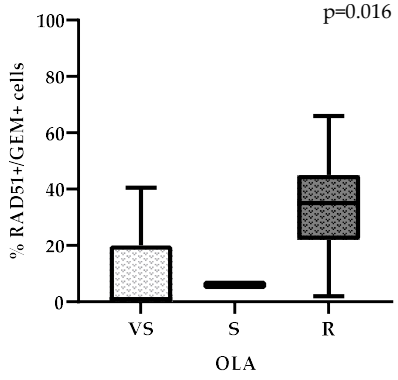

C

	For DDP response	For OLA response
Positive Predictive Value (PPV)	81.25%	75.00%
Negative Predictive Value (NPV)	25.00%	85.71%
Accuracy	50.00%	81.82%

Figure S3. % of RAD51+/GMN+ cells and response to cisplatin and olaparib in the high-grade OC-PDX subgroup

Panel A and B. Box plots show the correlation between the % of RAD51+/GMN+ cells and response to DDP (A) and olaparib (B) in the subgroup of high-grade OC-PDXs. *Panel C*. Positive and negative predictive values with accuracy of RAD51 test and DDP and olaparib response calculated in high-grade OC-PDXs.

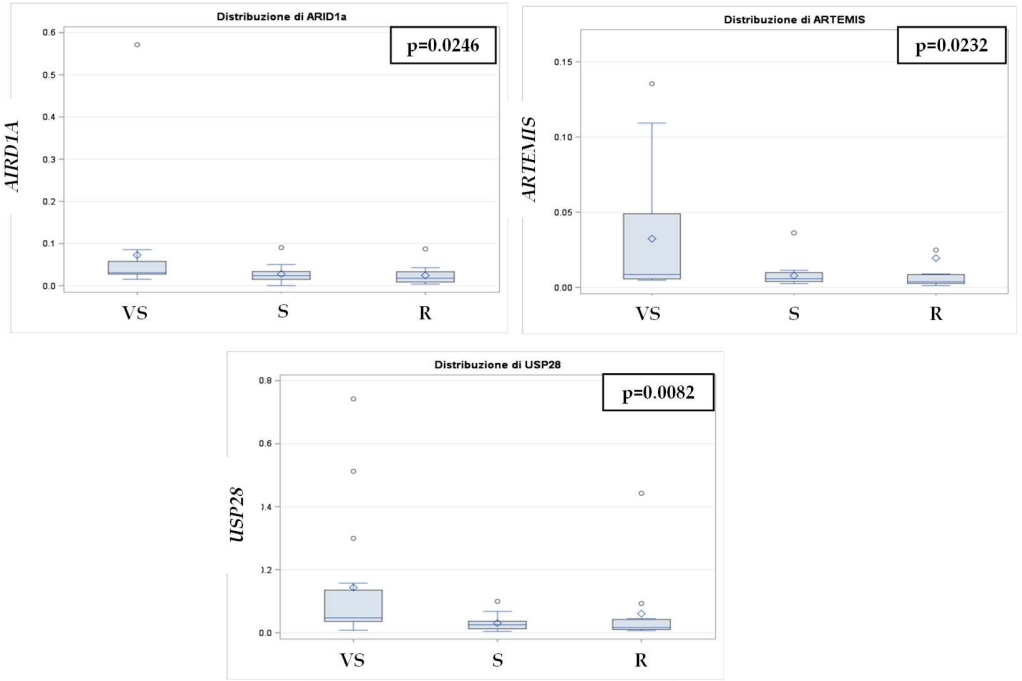

Figure S4. Genes whose mRNA expression level was significantly associated with DDP response in the OC-xenobank

Box plots showing the ARID1A, ARTEMIS and USP28 mean (diamond) and median (line) of the mRNA molecules expressed in all the PDXs classified by their response to DDP: very sensitive (VS), sensitive (S) and resistant (R). $p<0.05$. mRNA copies were calculated as the average of mRNA copies of three biological replicates normalized. Dots, outliers.

Table S1. List of the OC-PDXs with the histotype and site of tumor transplantation

		Tumor inoculum		Drug response	
#ID PDXs	Hystotype	s.c.	i.p.	DDP	OLA
MNHOC508	HGOC	X		VS	VS
MNHOC511	HGOC	X		VS	VS
MNHOC513	HGOC	X		VS	VS
MNHOC500	HGOC	X		VS	VS
MNHOC212	HGOC	X		VS	
MNHOC218	HGOC	X		VS	VS
MNHOC230	HGOC	X		VS	
MNHOC124	HGOC	X		VS	R
MNHOC316	HGOC	X		VS	R
MNHOC271	HGOC	X		S	S
MNHOC18	HGOC	X		S	R
MNHOC84	HGOC	X		S	R
MNHOC143	HGOC	X		S	R
MNHOC239	HGOC	X		S	R
MNHOC94/2C	LG	X		R	R
MNHOC94/2TR	HGOC	X		R	R
MNHOC124 ddpR	HGOC	X		R	R
MNHOC182	LG	X		R	R
MNHOC239 ddpR	HGOC	X		R	R
MNHOC315	HGOC	X		R	R
MNHOC241	LG	X		VS	
MNHOC261	HGOC	X		VS	
MNHOC9	HGOC	X		S	
MNHOC106	HGOC	X		S	
MNHOC107	HGOC	X		S	
MNHOC109	LG	X		S	
MNHOC125	HGOC	X		S	
MNHOC135	LG	X		S	
MNHOC154	HGOC	X		S	
MNHOC164	LG	X		S	
MNHOC258	HGOC	X		S	
MNHOC503	HGOC	X		S	
MNHOC119	LG	X		R	
MNHOC518	HGOC		X	VS	VS
MNHOC8	HGOC		X	VS	VS
MNHOC22	HGOC		X	VS	R
MNHOC506	HGOC		X	VS	R
MNHOC266	HGOC		X	VS	R
MNHOC520	HGOC		X	S	R
MNHOC266 ddpR	HGOC		X	R	R
MNHOC76	HGOC		X	R	R
MNHOC8R	HGOC		X	S	
MNHOC78	HGOC		X	S	
MNHOC142	LG		X	S	
MNHOC8Y	HGOC		X	R	
MNHOC10	HGOC		X	R	
MNHOC79	LG		X	R	
MNHOC111/2C	HGOC		X	R	

Abbreviations: HGOC= high grade ovarian cancer; LG= low grade ovarian cancer; s.c.= subcutaneos; i.p.= intraperitoneal; DDP= cisplatin; OLA= olaparib; VS= very sensitive; S= sensitive; R= resistant

Table S2. List of primers used for real time PCR

Gene	Primer Forward (5'->3')	Primer Reverse (5'->3')
ACTIN	TCACCCACACTGTGCCCATCTACGA	CAGCGGAACCGCTCATTGCCAATGG
CYP	GACCCAACACAAATGGTTCC	TTTCACTTTGCCAAACACCA
BRCA1	AGAAAGAGGAACGGGCTTGG	GACGCTTGTTTCACTCTCACAC
BRCA2	TGTCACAACCGTGTGGAAGT	TGATGGACGCCAAATACTCA
PARP1	AAGAAATGCAGCGAGAGCAT	CCAGTGTGGGACTTTTCCAT
RAD51	CAGATGCAGCTTGAAGCAAA	TTCTTCACATCGTTGGCATT
OGGI	CTCCACTCCTGCCCTGTG	CCAGTGTGCAGGACTTTGC
POLQ	GCTGGAACTTTTGCTGACCA	TCATGCCAACGATTTGCACA
CCNE1	AATGCGAGCAATTCTTCTGG	CGCCATATACCGGTCAAAGA
DNAPK	GCACTTTCAGCCCTGGAATC	CTGCTCCATAAAGTACTGCAGT
KU70	GCTTCTGCCTAGCGATACCA	CCCATGAGCATCAAACCTGG
KU80	TGAGAAGACAGACACCCTTGA	CCGGGGATGTAAAGCTCTGT
ARID1a	GTGTTGCTCAGTCTCGCTCA	ATTGGTTCATGGAAGGATGC
ARTEMIS	ACAGGAGACTTCAGATTGGCG	CACTCCTCCCGACTTGGAATT
CHD4	ACCCAAGAAAGTAGCTCCCC	ACTGGCATCATCGAAGTCAGA
MDR1	CCCATCATTGCAATAGCAGG	GTTCAAACTTCTGCTCCTGA
PTIP	AGGAAAGCCATGTTCACAGC	CACCTGCCAAATAAGCCATT
RAD51C	GCCTTGCTTGTTCCTGCATT	TGGCTGGGTGACTTGTACAA
REV7	AGTGGTGGTGGTGATTTTGG	AGCTGCTCCACATGAGACAA
SLFN11	TGGGTAGGCATGATGACAGA	AAGGGGAGGCCCACTAGATA
TP53BP1	TGGTTCCATCAGTCAGGTCA	ACAGCAGGAGCAGATTCCAC
USP28	AGTGCTGCCAACAAGGAAGT	TTGAATTTTGGGAGACTCCAG
CARM1	ATCCGGATCCTGATGGCCA	AGCAACGTCAAACCAGAAAGC

List of primers used for *BRCA1* methylation specific PCR

Primer Name	Primer Forward (5'->3')	Primer Reverse (5'->3')
BRCA1 Methylated (M)	TCGTGGTAACGGAAAAGCGC	AAATCTCAACGAACTCACGCCG
BRCA1 Unmethylated (U)	TTGGTTTTTGTGGTAATGGAAAAGTGT	CAAAAAATCTCAACA AACTCACACCA
Calponin	GGAAGGTAGTTGAGGTTGTG	CCCAAACTCAAAACTCTAACCT

Table S3. mRNA copy number of different DNA repair-related genes normalized by housekeeping genes

#ID PDXs	*BRCA1*	*BRCA2*	*PARP1*	*RAD51*	*OGG1*	*POLQ*	*CCNE1*	*DNAPK*	*KU70*	*KU80*	*ARID1a*	*ARTEMIS*	*CHD4*	*MDR1*	*PTIP*	*RAD51C*	*REV7*	*SLFN11*	*TP53BP1*	*USP28*	*CARM1*
MNHOC508	0.07280	0.00283	0.02893	0.08466	0.01421	0.02028	0.15834	0.14135	0.10501	0.03101	0.07489	0.09771	0.17125	0.00005	0.07662	0.01760	0.16911	0.06278	0.87085	0.29962	0.00367
MNHOC511	0.00235	0.01279	0.19719	0.00724	0.07165	0.92757	0.26040	0.15356	0.02796	0.12590	0.02587	0.00480	0.03943	0.00002	0.00517	0.01795	0.03527	0.00064	0.09536	0.03799	0.00419
MNHOC513	0.01695	0.01366	0.05109	0.01551	0.05459	0.01621	0.01336	0.27585	0.19031	0.08546	0.08539	0.05072	0.44411	0.00004	0.05120	0.03039	0.87212	0.10383	0.85326	0.51226	0.00365
MNHOC500	0.05210		0.09319	0.24399	0.01354	0.10273	0.22113	0.17854	0.05583	0.13530	0.01525	0.00889	0.04879	0.00003	0.00630	0.02665	0.01149	0.01205	0.28969	0.02580	0.00352
MNHOC212	0.00017		2.36206	3.71412	0.65091	4.02970	0.15799	0.13165	0.06335	0.09963	0.02738	0.00586	0.04691	0.00001	0.00669	0.01304	0.02582	0.03970	0.14717	0.10379	0.00968
MNHOC218	0.00867	0.00685	0.02854	0.07353	0.00281	0.02950	0.00698	0.20364	0.09903	0.04679	0.04286	0.10924	0.23193	0.00010	0.04916	0.00788	0.15567	0.02470	0.25270	0.11306	0.00399
MNHOC230	0.03162		0.04392	0.05394	0.01194	0.03482	0.13596	0.12557	0.03754	0.05686	0.03157	0.00819	0.04780	0.00014	0.02134	0.03138	0.05005	0.01383	0.23616	0.06116	0.01722
MNHOC124	0.07464	0.00936	0.01202	0.08461	0.00620	0.08358	0.05250	0.12743	0.03007	0.15762	0.03284	0.00541	0.04202	0.00004	0.01849	0.02126	0.02894	0.01450	0.24022	0.03739	0.01818
MNHOC316	0.00482	0.00641	0.01642	0.00372	0.02181	0.01100	0.01073	0.10052	0.06257	0.02973	0.06864	0.04719	0.13748	0.00004	0.01238	0.01600	0.16172	0.02911	0.20864	0.15706	0.00349
MNHOC271	0.00476	0.00378	0.03193	0.00680	0.02244	0.01459	0.11342	0.06635	0.05809	0.10526	0.00902	0.00382	0.02544	0.00004	0.00693	0.01657	0.01860	0.00027	0.15845	0.02653	0.00536
MNHOC18	0.06193		0.03889	0.13821	0.00717	0.04603	0.37130	0.34872	0.06902	0.10161	0.02422	0.00454	0.06021	0.00001	0.00587	0.02404	0.03612	0.03627	0.26563	0.00404	0.01021
MNHOC84	0.03685		0.00631	0.02357	0.00208	0.01676	0.00511	0.13608	0.06193	0.15608	0.01291	0.00442	0.03243	0.00006	0.00173	0.01544	0.01195	0.00899	0.06662	0.01165	0.00495
MNHOC143	0.04331		0.06713	0.11185	0.00516	0.02945	0.13783	0.05049	0.03568	0.04539	0.03377	0.00598	0.03992	0.00004	0.00339	0.01943	0.01578	0.02850	0.25535	0.02341	0.00601
MNHOC239	0.04490	0.02130	0.05554	0.11381	0.00884	0.06226	0.24475	0.40561	0.08259	0.10345	0.02571	0.00504	0.06064	0.00002	0.00839	0.01993	0.09122	0.03359	0.38802	0.02354	0.00805
MNHOC94/2C	0.06298		0.01070	0.07498	0.00505	0.03246	0.55950	0.08577	0.05582	0.04767	0.00936	0.00126	0.03350	0.00003	0.00743	0.00617	0.01013	0.00007	0.17184	0.02591	0.00277
MNHOC124 ddpR	0.03871	0.02870	0.55809	0.01458	0.15339	0.54638	0.02456	0.21609	0.08619	0.15593	0.00745	0.00345	0.06904	0.00004	0.01435	0.00798	0.05280	0.00051	0.13005	0.01593	0.01577
MNHOC182	0.04431		0.01791	0.09426	0.00230	0.03271	0.46463	0.12476	0.07045	0.09106	0.00812	0.00254	0.04458	0.00002	0.00767	0.00814	0.03344	0.00465	0.20820	0.01044	0.00723
MNHOC239 ddpR	0.02032	0.02042	0.74990	0.00659	0.16111	0.25079	0.06227	0.73355	0.13800	0.11202	0.01348	0.00807	0.12382	0.00001	0.00812	0.00909	0.13194	0.00920	0.16204	0.01638	0.02016
MNHOC315	0.00035	0.00356	0.08497	0.00381	0.02378	0.02871			0.02849		0.00378	0.00200	0.01750	0.00002	0.00381	0.01175	0.01941	0.00500	0.14007	0.00983	0.00616
MNHOC241	0.05924		0.04370	0.06063	0.01350	0.03558	0.33204	0.18306	0.06190	0.13916	0.03058	0.00811	0.09693	0.00006	0.01066	0.03676	0.03046	0.00525	0.33821	0.04471	0.01429
MNHOC261	0.04348		0.03888	0.05853	0.01318	0.02734	0.05020	0.28731	0.02638	0.21077	0.04676	0.01078	0.14527	0.00006	0.00926	0.03172	0.08522	0.02763	0.34191	0.04925	0.00419
MNHOC9	0.05227		0.01945	0.09768	0.00633	0.10523	0.15764	0.10002	0.03579	0.08767	0.03269	0.01080	0.04942	0.00001	0.01484	0.03746	0.08030	0.01510	0.19494	0.04125	0.00461
MNHOC106	0.03868		0.05546	0.10051	0.01255	0.07984	0.22894	0.18360	0.09310	0.13193	0.02236	0.00584	0.04840	0.00001	0.01124	0.02034	0.02881	0.00381	0.06883	0.03568	0.00371
MNHOC107	0.03022		0.03046	0.11321	0.00376	0.05960	0.25862	0.09412	0.04497	0.04775	0.00044	0.00386	0.03171	0.00001	0.01196	0.01198	0.01770	0.00436	0.13414	0.03605	0.00647
MNHOC109	0.03920		0.01157	0.05167	0.00199	0.02625	0.09865	0.04323	0.05678	0.09568	0.00760	0.00251	0.01811	0.00002	0.00541	0.01738	0.02179	0.00001	0.09098	0.01241	0.00608
MNHOC125	0.08466		0.02291	0.15684	0.00435	0.04389	0.10724	0.04984	0.03460	0.03209	0.02355	0.00572	0.05557	0.00004	0.00462	0.02759	0.01800	0.00612	0.30025	0.02069	0.00782
MNHOC135	0.14488		0.08045	0.11555	0.00723	0.10832	0.17370	0.27585	0.09615	0.29771	0.03986	0.01140	0.14781	0.00006	0.00624	0.00092	0.02996	0.01024	0.31659	0.03645	0.01766
MNHOC154	0.07554		0.03625	0.09095	0.01140	0.04540	0.64489	0.22885	0.07713	0.29161	0.09049	0.00734	0.10610	0.00002	0.02753	0.03507	0.07324	0.00019	0.34573	0.01226	n/a
MNHOC164	0.03981		0.00817	0.02781	0.00208	0.01088	0.06007	0.10211	0.04862	0.06416	0.01507	0.00316	0.01153	0.00004	0.01069	0.02421	0.01509	0.10361	0.06928	0.00884	0.00504
MNHOC258	0.05097		0.02052	0.06098	0.00659	0.05326	0.45919	0.23366	0.05877	0.21312	0.03026	0.00979	0.09446	0.00001	0.01193	0.03470	0.03674	0.02884	0.21764	0.06740	0.00940
MNHOC503	0.04108		0.04212	0.06304	0.00541	0.02344					0.02160	0.00339	0.03961	0.00228	0.00867	0.01275	0.02353	0.01038	0.19694	0.00987	0.00788
MNHOC119	0.05336		0.00758	0.10128	0.00357	0.02940	0.18430	0.10741	0.04618	0.06206	0.00939	0.00282	0.01760	0.00000	0.00378	0.01019	0.02221	0.00008	0.10995	0.01043	0.00611
MNHOC518	0.01894	0.02408	0.22144	0.07530	0.11525	0.03677	0.01830	1.18331	0.52605	0.16845	0.57119	0.13541	1.14562	undetermined	0.07591	0.09115	1.76456	0.14464	3.11163	0.74196	0.00441
MNHOC8	0.00377		0.03030	0.33645	0.00965	0.07919	0.19140	0.31532	0.05846	0.16605	0.02859	0.00479	0.07219	0.00001	0.01314	0.01919	0.07332	0.00060	0.19781	0.03385	0.01043
MNHOC22	0.04462		0.04703	0.12237	0.01260	0.09204	0.27384	0.19933	0.07587	0.12303	0.02817	0.00608	0.05233	0.00001	0.00786	0.03023	0.05265	0.00363	0.19144	0.03119	0.00773
MNHOC506	0.05463		0.02282	0.05786	0.00463	0.02096	0.43076	0.06930	0.02864	0.09089	0.02257	0.00535	0.03438	0.00002	0.00468	0.01608	0.00711	0.01219	0.14159	0.00758	0.01255
MNHOC266	0.03445	0.00256	0.03270	0.06117	0.00764	0.04584	0.15649	0.67738	0.09287	0.16813	0.03009	0.00889	0.09276	0.00001	0.01755	0.06850	0.03846	0.01664	0.53021	0.03921	0.01351
MNHOC520	0.00157	0.00086	0.01893	0.00316	0.02308	0.00260	0.00189	0.08539	0.10035	0.02935	0.05034	0.03620	0.17001	0.00000	0.01429	0.00600	0.16480	0.01698	0.36098	0.09939	0.00278
MNHOC266 ddpR	0.04792	0.01410	0.04178	0.01975	0.08831	0.07404	0.01511	1.02562	0.13118	0.05434	0.08710	0.16746	0.74308	0.00003	0.06009	0.04326	1.01901	0.09906	1.63339	0.44255	0.00312
MNHOC76	0.03289	0.00189	0.01673	0.02975	0.00537	0.02497	0.25864	0.16763	0.10797	0.10464	0.02874	0.02485	0.10856	0.00003	0.01068	0.01929	0.18664	0.01801	0.14427	0.09263	0.00145
MNHOC78	0.07407		0.01711	0.07347	0.01653	0.04231	0.12751	0.17781	0.02528	0.19656	0.04195	0.00987	0.04227	0.00005	0.01028	0.04133	0.20296	0.00565	0.22424	0.04990	0.00803
MNHOC142	0.10841		0.01617	0.14385	0.01800	0.08788	0.39762	0.05859	0.09353	0.10228	0.02159	0.00634	0.04195	0.00001	0.01110	0.01142	0.02796	0.00016	0.46663	0.02878	0.00326
MNHOC8Y	0.00042		0.04223	0.47666	0.01878	0.09656	0.28357	0.24879	0.07637	0.18954	0.03775	0.00570	0.09724	0.00000	0.01711	0.02109	0.11351	0.00103	0.14758	0.03941	0.01384
MNHOC10	0.02468		0.01653	0.07327	0.00639	0.03612	0.16024	0.07983	0.04957	0.09066	0.02525	0.00399	0.06723	0.00001	0.00544	0.02742	0.03487	0.01764	0.17371	0.00811	0.01281
MNHOC79	0.04990		0.04447	0.10582	0.00420	0.03645	0.59650	0.06185	0.03759	0.05625	0.04281	0.00318	0.04556	0.00000	0.00620	0.01719	0.02782	0.00001	0.16371	0.00634	0.00426
MNHOC111/2C	0.13151		0.03316	0.21658	0.00631	0.05473	0.14060	0.25887	0.05880	0.27922	0.02232	0.00890	0.12756	0.00000	0.01287	0.02577	0.04525	0.01607	0.66534	0.04438	0.01064

Table S4. BRCA1 mRNA levels in BRCA1 promoter hyper-methylated vs unmethylated OC-PDXs

#ID PDXs	%CpG islands methylated in *BRCA1* promoter	Mean and st. dev. of BRCA1 normalized mRNA quantity in hyper-methylated PDXs	Mean and st. dev. of BRCA1 normalized mRNA quantity in unmethylated PDXs	p-value
MNHOC212	100%	0.0058 ±0,01	0.0472 ±0,03	0.0013
MNHOC8	84%			
MNHOC8Y	100%			
MNHOC518	100%			

Table S5. CCNE1 gene copy number variation and number of mRNA molecules expressed in the OC-PDXs

#ID PDXs	DDP	*CCNE1* CNV	CCNE1 normalized mRNA quantity	Mean ± st. dev. CCNE1 normalized mRNA quantity
MNHOC79	Resistant	2	0.59650	0,229±0,21
MNHOC94/2C		2	0.55950	
MNHOC182		2	0.46463	
MNHOC8Y		2	0.28357	
MNHOC76		2	0.25864	
MNHOC119		4 (*)	0.18430	
MNHOC10		2	0.16024	
MNHOC84		2	0.00511	
MNHOC111/2C		2	0.14060	
MNHOC239 ddpR		1	0.06227	
MNHOC124 ddpR		2	0.02456	
MNHOC266 ddpR		3	0.01511	
MNHOC94/2TR		3	-	
MNHOC315		2	-	
MNHOC154	Sensitive	2	0.64489	0,224±0,17
MNHOC258		2	0.45919	
MNHOC142		2	0.39762	
MNHOC18		5 (*)	0.37130	
MNHOC107		1	0.25862	
MNHOC239		2	0.24475	
MNHOC106		3	0.22894	
MNHOC135		2	0.17370	
MNHOC9		2	0.15764	
MNHOC143		2	0.13783	
MNHOC78		2	0.12751	
MNHOC271		2	0.11342	
MNHOC125		2	0.10724	
MNHOC109		2	0.09865	
MNHOC164		5 (*)	0.06007	
MNHOC520		3	0.00189	
MNHOC503		2	-	
MNHOC506	Very sensitive	2	0.43076	0,154 ±0,13
MNHOC241		2	0.33204	
MNHOC22		2	0.27384	
MNHOC511		3	0.26040	
MNHOC500		2	0.22113	
MNHOC8		-	0.19140	
MNHOC508		2	0.15834	
MNHOC212		2	0.15799	
MNHOC266		2	0.15649	
MNHOC230		2	0.13596	
MNHOC124		2	0.05250	
MNHOC261		2	0.05020	
MNHOC518		2	0.01830	
MNHOC513		2	0.01336	
MNHOC316		2	0.01073	
MNHOC218		2	0.00698	