

9464	FOXO1 (T24)/FOXO3 (T32)	CellSig	1:200	R
9331	GSK-3a/B (S21/9)	CellSig	1:100	R
9246	IkappaB-alpha (S32/36)	CellSig	1:100	M
2386	IRS-1 (S612)	CellSig	1:200	R
3391	c-Kit (Y719)	CellSig	1:250	R
34-9400	c-Kit (Y721)	Invitrogen	1:200	R
2741	MARCKS (S152/156)	CellSig	1:200	R
9121	MEK1/2 (S217/221)	CellSig	1:500	R
3126	Met (Y1234/1235)	CellSig	1:200	R
2971	mTOR (S2448)	CellSig	1:100	R
2974	mTOR (S2481)	CellSig	1:100	R
3031	NF-kappaB p65 (S536)	CellSig	1:100	R
9211	p38 MAPK (T180/Y182)	CellSig	1:100	R
9208	p70 S6 Kinase (S371)	CellSig	1:50	R
9341	p90RSK (S380)	CellSig	1:400	R
4781	PKA C (T197)	CellSig	1:200	M
06-822	PKC alpha (S657)	Millipore	1:1000	R
9374	PKC delta (T505)	CellSig	1:50	R
9378	PKC zeta/lambda (T410/403)	CellSig	1:50	R
44-1100	PRAS40 (T246)	Invitrogen	1:1000	R
9551	PTEN (S380)	CellSig	1:500	R
4431	A-Raf (S299)	CellSig	1:100	R
2696	B-Raf (S445)	CellSig	1:50	R
9427	C-Raf (S338)	CellSig	1:200	R
3321	Ras-GRF1 (S916)	CellSig	1:50	R
9251	SAPK/JNK (T183/Y185)	CellSig	1:200	R
07-206	Shc (Y317)	Millipore	1:200	R
2954	Smac/Diablo	CellSig	1:1000	R
3101	SMAD2 (S465/467)	CellSig	1:250	R
9134	Stat3 (S727)	CellSig	1:100	R
05-485	Stat3 (Y705)	Millipore	1:200	R
9351	Stat5 (Y694)	CellSig	1:50	R
9361	Stat6 (Y641)	CellSig	1:100	R
2478	VEGFR 2 (Y1175)	CellSig	1:50	R
	Abbreviations: R: rabbit; M: mouse. Cell Signaling			
	Technology, Inc, Danvers, MA, USA.Millipore,			

Billerica, MA, USA. BD biosciences, Franklin Lakes, NJ, USA. Invitrogen, Carlsbad, CA, USA. Dako Inc, Carpinteria, CA, USA

Supplementary Table 2

Total, cleaved (cl) or phosphorylated protein expression in lapatinib-treated ZR-75-1-derived cell lines

Antibodies used are specified in Supplementary Table 1

Expression levels (AU, arbitrary units, average of triplicates) were normalised to total protein.

Values above 700 have a CV of less than 2% across the triplicates

Relative expression levels (R) are relative to estradiol-treated ZR/vector cells

(E2), estradiol; (4-OHT), 4-hydroxytamoxifen. Cells treated without (0 μ M), or with 0.01 μ M or 0.1 μ M lapatinib for 17h.

Sample Name	EIF4EBP1		ABL1 T735		ACC S79		ADD		AKT (S473)		AKT (T308)		PRKAA1		PRKAB1		BAX	
	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	31257	1.0	3378	1.0	11464	1.0	8030	1.0	139	1.0	685	1.0	313	1.0	4016	1.0	2189	1.0
ZR/vector (E2) 0.01 μ M	32209	1.0	3667	1.1	9443	0.8	8734	1.1	193	1.4	1732	2.5	583	1.9	4205	1.0	2128	1.0
ZR/vector (E2) 0.1 μ M	30946	1.0	3572	1.1	8911	0.8	8103	1.0	9	0.1	1604	2.3	0	0.0	3502	0.9	1494	0.7
ZR/BCAR4 (E2) 0 μ M	44802	1.4	4910	1.5	5541	0.5	12457	1.6	3816	27.5	1937	2.8	0	0.0	7080	1.8	1799	0.8
ZR/BCAR4 (E2) 0.01 μ M	25591	0.8	4760	1.4	10077	0.9	5362	0.7	334	2.4	1672	2.4	0	0.0	3100	0.8	3072	1.4
ZR/BCAR4 (E2) 0.1 μ M	37049	1.2	4452	1.3	10148	0.9	6884	0.9	1471	10.6	812	1.2	364	1.2	4856	1.2	2876	1.3
ZR/BCAR4 (4-OHT) 0 μ M	48533	1.6	3984	1.2	7037	0.6	11743	1.5	19970	144.2	3882	5.7	4920	15.7	5979	1.5	1682	0.8
ZR/BCAR4 (4-OHT) 0.01 μ M	44802	1.4	3678	1.1	6884	0.6	13095	1.6	20313	146.6	2945	4.3	5665	18.1	6575	1.6	1835	0.8
ZR/BCAR4 (4-OHT) 0.1 μ M	35596	1.1	3767	1.1	11294	1.0	11556	1.4	12259	88.5	1826	2.7	6021	19.3	8283	2.1	2006	0.9
ZR/BCAR3 (E2) 0 μ M	25848	0.8	5105	1.5	20313	1.8	9045	1.1	835	6.0	456	0.7	430	1.4	6342	1.6	3023	1.4
ZR/BCAR3 (E2) 0.01 μ M	24835	0.8	4770	1.4	14780	1.3	8193	1.0	872	6.3	276	0.4	241	0.8	6850	1.7	2419	1.1
ZR/BCAR3 (E2) 0.1 μ M	23156	0.7	4068	1.2	14214	1.2	7223	0.9	1042	7.5	881	1.3	1407	4.5	5182	1.3	1852	0.8
ZR/BCAR3 (4-OHT) 0 μ M	22925	0.7	4930	1.5	17748	1.5	10457	1.3	6905	49.8	1916	2.8	3752	12.0	5779	1.4	2082	1.0
ZR/BCAR3 (4-OHT) 0.01 μ M	22248	0.7	4750	1.4	11545	1.0	9858	1.2	6368	46.0	1240	1.8	3519	11.3	4895	1.2	1583	0.7
ZR/BCAR3 (4-OHT) 0.1 μ M	21590	0.7	4619	1.4	14574	1.3	11453	1.4	6595	47.6	1647	2.4	4176	13.4	5298	1.3	1591	0.7
ZR/EGFR (E2) 0 μ M	47099	1.5	4934	1.5	17223	1.5	6477	0.8	302	2.2	428	0.6	1037	3.3	6581	1.6	2294	1.0
ZR/EGFR (E2) 0.01 μ M	40135	1.3	4573	1.4	13004	1.1	5991	0.7	275	2.0	547	0.8	749	2.4	4784	1.2	2105	1.0
ZR/EGFR (E2) 0.1 μ M	43478	1.4	4638	1.4	15429	1.3	6051	0.8	290	2.1	747	1.1	638	2.0	6075	1.5	2482	1.1
ZR/EGFR (4-OHT + EGF) 0 μ M	46630	1.5	6634	2.0	17908	1.6	8111	1.0	906	6.5	674	1.0	2145	6.9	6361	1.6	1405	0.6
ZR/EGFR (4-OHT + EGF) 0.01 μ M	51021	1.6	6535	1.9	15367	1.3	7685	1.0	1253	9.0	874	1.3	2101	6.7	5914	1.5	1384	0.6
ZR/EGFR (4-OHT + EGF) 0.1 μ M	42193	1.3	6412	1.9	13753	1.2	6748	0.8	1086	7.8	374	0.5	1498	4.8	4592	1.1	1112	0.5

Sample Name	BCL2 (T56)		BCL2 (S70)		CASP 8		CASP3 cl		CASP7 cl		CASP9 cl		CTNBB1		CREB		Cyclin A	
	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μM	1103	1.0	2592	1.0	2553	1.0	1984	1.0	3948	1.0	3590	1.0	455	1.0	1491	1.0	1494	1.0
ZR/vector (E2) 0.01 μM	984	0.9	896	0.3	2708	1.1	1626	0.8	4429	1.1	2893	0.8	642	1.4	1561	1.0	1785	1.2
ZR/vector (E2) 0.1 μM	444	0.4	1331	0.5	2639	1.0	1354	0.7	3786	1.0	2819	0.8	623	1.4	1828	1.2	1326	0.9
ZR/BCAR4 (E2) 0 μM	857	0.8	881	0.3	2755	1.1	1662	0.8	3741	0.9	3159	0.9	883	1.9	2940	2.0	2458	1.6
ZR/BCAR4 (E2) 0.01 μM	610	0.6	1644	0.6	2870	1.1	4130	2.1	7187	1.8	3415	1.0	566	1.2	1947	1.3	1696	1.1
ZR/BCAR4 (E2) 0.1 μM	1053	1.0	1488	0.6	2864	1.1	3159	1.6	4605	1.2	3689	1.0	756	1.7	2122	1.4	1667	1.1
ZR/BCAR4 (4-OHT) 0 μM	854	0.8	1880	0.7	2269	0.9	4827	2.4	4205	1.1	2553	0.7	838	1.8	3565	2.4	1621	1.1
ZR/BCAR4 (4-OHT) 0.01 μM	1060	1.0	1961	0.8	2568	1.0	5378	2.7	4311	1.1	3084	0.9	1002	2.2	3580	2.4	1651	1.1
ZR/BCAR4 (4-OHT) 0.1 μM	1447	1.3	2315	0.9	2571	1.0	7391	3.7	6933	1.8	3641	1.0	923	2.0	4000	2.7	1289	0.9
ZR/BCAR3 (E2) 0 μM	772	0.7	1561	0.6	3321	1.3	3294	1.7	4324	1.1	3921	1.1	764	1.7	1722	1.2	1410	0.9
ZR/BCAR3 (E2) 0.01 μM	852	0.8	1132	0.4	2963	1.2	3328	1.7	3909	1.0	3855	1.1	740	1.6	2122	1.4	1636	1.1
ZR/BCAR3 (E2) 0.1 μM	1162	1.1	1391	0.5	2165	0.8	3707	1.9	3544	0.9	2470	0.7	804	1.8	1776	1.2	1060	0.7
ZR/BCAR3 (4-OHT) 0 μM	939	0.9	1710	0.7	2779	1.1	5597	2.8	4817	1.2	3294	0.9	1028	2.3	2993	2.0	1297	0.9
ZR/BCAR3 (4-OHT) 0.01 μM	870	0.8	1494	0.6	2061	0.8	5095	2.6	4483	1.1	2350	0.7	1090	2.4	2470	1.7	1141	0.8
ZR/BCAR3 (4-OHT) 0.1 μM	1066	1.0	1810	0.7	2543	1.0	5156	2.6	4684	1.2	2975	0.8	1008	2.2	3072	2.1	1220	0.8
ZR/EGFR (E2) 0 μM	1293	1.2	1830	0.7	2576	1.0	4109	2.1	3495	0.9	2893	0.8	963	2.1	2571	1.7	1272	0.9
ZR/EGFR (E2) 0.01 μM	1201	1.1	1602	0.6	2373	0.9	3782	1.9	3477	0.9	2887	0.8	829	1.8	2137	1.4	1032	0.7
ZR/EGFR (E2) 0.1 μM	901	0.8	1358	0.5	2594	1.0	3913	2.0	3210	0.8	2668	0.7	759	1.7	2156	1.4	1135	0.8
ZR/EGFR (4-OHT + EGF) 0 μM	1666	1.5	1744	0.7	2152	0.8	4803	2.4	3805	1.0	3184	0.9	927	2.0	3944	2.6	1265	0.8
ZR/EGFR (4-OHT + EGF) 0.01 μM	1454	1.3	1588	0.6	2169	0.8	4944	2.5	3771	1.0	2641	0.7	1044	2.3	3767	2.5	1229	0.8
ZR/EGFR (4-OHT + EGF) 0.1 μM	1638	1.5	1321	0.5	1951	0.8	4555	2.3	3980	1.0	2545	0.7	982	2.2	3358	2.3	1264	0.8

Sample Name	Cyclin D1		Cyclin E		total EGFR		EIF4G		eNOS-NOSIII		Total ESR1		ESR1		total ERBB2		ERBB2	
	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	6223	1.0	4320	1.0	183	1.0	4201	1.0	5569	1.0	2222	1.0	3255	1.0	4974	1.0	2239	1.0
ZR/vector (E2) 0.01 μ M	7716	1.2	5146	1.2	222	1.2	5410	1.3	7080	1.3	2573	1.2	3960	1.2	7339	1.5	2636	1.2
ZR/vector (E2) 0.1 μ M	7495	1.2	5287	1.2	626	3.4	4798	1.1	6173	1.1	2470	1.1	3816	1.2	6112	1.2	2847	1.3
ZR/BCAR4 (E2) 0 μ M	12506	2.0	10178	2.4	1169	6.4	9557	2.3	6529	1.2	1527	0.7	4167	1.3	3565	0.7	27447	12.3
ZR/BCAR4 (E2) 0.01 μ M	7990	1.3	6549	1.5	99	0.5	2376	0.6	5448	1.0	1383	0.6	3752	1.2	10583	2.1	3298	1.5
ZR/BCAR4 (E2) 0.1 μ M	8604	1.4	7480	1.7	337	1.8	4496	1.1	4939	0.9	1732	0.8	3667	1.1	9789	2.0	5608	2.5
ZR/BCAR4 (4-OHT) 0 μ M	10775	1.7	5745	1.3	351	1.9	8160	1.9	7700	1.4	1028	0.5	2347	0.7	10797	2.2	20640	9.2
ZR/BCAR4 (4-OHT) 0.01 μ M	12734	2.0	6198	1.4	445	2.4	8493	2.0	8493	1.5	1112	0.5	2455	0.8	14988	3.0	21248	9.5
ZR/BCAR4 (4-OHT) 0.1 μ M	11580	1.9	5855	1.4	352	1.9	7194	1.7	8760	1.6	1146	0.5	2324	0.7	27447	5.5	10808	4.8
ZR/BCAR3 (E2) 0 μ M	7087	1.1	8442	2.0	59	0.3	8242	2.0	5525	1.0	2167	1.0	4286	1.3	15662	3.1	4105	1.8
ZR/BCAR3 (E2) 0.01 μ M	6926	1.1	8039	1.9	311	1.7	6775	1.6	5453	1.0	2043	0.9	3984	1.2	19811	4.0	3928	1.8
ZR/BCAR3 (E2) 0.1 μ M	5313	0.9	4474	1.0	253	1.4	7016	1.7	4394	0.8	1306	0.6	2540	0.8	19341	3.9	4126	1.8
ZR/BCAR3 (4-OHT) 0 μ M	6884	1.1	6003	1.4	296	1.6	7281	1.7	7495	1.3	1753	0.8	2485	0.8	27447	5.5	6581	2.9
ZR/BCAR3 (4-OHT) 0.01 μ M	5802	0.9	5115	1.2	197	1.1	6003	1.4	7739	1.4	1196	0.5	2084	0.6	26370	5.3	5710	2.5
ZR/BCAR3 (4-OHT) 0.1 μ M	6069	1.0	5470	1.3	129	0.7	6368	1.5	8063	1.4	1612	0.7	2303	0.7	28001	5.6	6229	2.8
ZR/EGFR (E2) 0 μ M	8201	1.3	5287	1.2	16631	91.0	7274	1.7	5855	1.1	1317	0.6	2211	0.7	5187	1.0	2165	1.0
ZR/EGFR (E2) 0.01 μ M	6267	1.0	4523	1.0	15804	86.5	4642	1.1	5525	1.0	1424	0.6	2477	0.8	6285	1.3	1974	0.9
ZR/EGFR (E2) 0.1 μ M	7274	1.2	5271	1.2	15678	85.8	5372	1.3	5855	1.1	1143	0.5	2830	0.9	5866	1.2	2222	1.0
ZR/EGFR (4-OHT + EGF) 0 μ M	12345	2.0	5872	1.4	26635	145.8	8144	1.9	8226	1.5	602	0.3	2084	0.6	12670	2.5	5004	2.2
ZR/EGFR (4-OHT + EGF) 0.01 μ M	10017	1.6	5054	1.2	24101	131.9	5687	1.4	8047	1.4	619	0.3	1980	0.6	14343	2.9	4959	2.2
ZR/EGFR (4-OHT + EGF) 0.1 μ M	9100	1.5	4832	1.1	22697	124.2	5100	1.2	8317	1.5	412	0.2	1939	0.6	14003	2.8	4959	2.2

Sample Name	ERBB3		total ERBB4		ERK1-2		FADD		FAK		FOXO1 (S256)		FOXO3 (S253)		FOXO1/3 (T24/32)		GSK3A/B	
	AU	R	AU	R	AU	R		R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	2421	1.0	4342	1.0	1043	1.0	10551	1.0	2612	1.0	3572	1.0	8578	1.0	1112	1.0	6575	1.0
ZR/vector (E2) 0.01 μ M	2251	0.9	5508	1.3	1256	1.2	12382	1.2	3175	1.2	4171	1.2	7420	0.9	1213	1.1	6933	1.1
ZR/vector (E2) 0.1 μ M	2438	1.0	4915	1.1	1193	1.1	11837	1.1	4101	1.6	3855	1.1	8647	1.0	1120	1.0	6211	0.9
ZR/BCAR4 (E2) 0 μ M	12481	5.2	5405	1.2	2147	2.1	15584	1.5	19380	7.4	6015	1.7	10604	1.2	7677	6.9	13440	2.0
ZR/BCAR4 (E2) 0.01 μ M	4765	2.0	4871	1.1	1564	1.5	6614	0.6	2948	1.1	4746	1.3	13671	1.6	1566	1.4	7624	1.2
ZR/BCAR4 (E2) 0.1 μ M	7700	3.2	5443	1.3	1358	1.3	8911	0.8	3748	1.4	4746	1.3	13280	1.5	2873	2.6	10711	1.6
ZR/BCAR4 (4-OHT) 0 μ M	17765	7.3	5508	1.3	983	0.9	17018	1.6	9256	3.5	4097	1.1	8630	1.0	6027	5.4	12040	1.8
ZR/BCAR4 (4-OHT) 0.01 μ M	18770	7.8	6674	1.5	832	0.8	16482	1.6	7731	3.0	4713	1.3	8725	1.0	6708	6.0	12040	1.8
ZR/BCAR4 (4-OHT) 0.1 μ M	20191	8.3	6919	1.6	808	0.8	14516	1.4	3767	1.4	4519	1.3	7723	0.9	7919	7.1	9585	1.5
ZR/BCAR3 (E2) 0 μ M	2628	1.1	5229	1.2	1132	1.1	14794	1.4	2326	0.9	4827	1.4	8217	1.0	2907	2.6	12247	1.9
ZR/BCAR3 (E2) 0.01 μ M	2329	1.0	5603	1.3	1207	1.2	13333	1.3	2338	0.9	4741	1.3	8691	1.0	2830	2.5	11328	1.7
ZR/BCAR3 (E2) 0.1 μ M	1839	0.8	4656	1.1	687	0.7	14883	1.4	1259	0.5	3685	1.0	8991	1.0	1937	1.7	9653	1.5
ZR/BCAR3 (4-OHT) 0 μ M	2257	0.9	6483	1.5	852	0.8	12978	1.2	1698	0.6	4934	1.4	8613	1.0	4910	4.4	8604	1.3
ZR/BCAR3 (4-OHT) 0.01 μ M	1610	0.7	6445	1.5	659	0.6	13121	1.2	1553	0.6	4247	1.2	9009	1.1	4793	4.3	6836	1.0
ZR/BCAR3 (4-OHT) 0.1 μ M	1476	0.6	7252	1.7	682	0.7	13069	1.2	1498	0.6	4294	1.2	8682	1.0	5710	5.1	8014	1.2
ZR/EGFR (E2) 0 μ M	2371	1.0	3882	0.9	1776	1.7	12506	1.2	1774	0.7	4113	1.2	12607	1.5	2078	1.9	6714	1.0
ZR/EGFR (E2) 0.01 μ M	2273	0.9	3809	0.9	966	0.9	9018	0.9	1507	0.6	3484	1.0	13056	1.5	1760	1.6	5497	0.8
ZR/EGFR (E2) 0.1 μ M	2269	0.9	3616	0.8	1450	1.4	9711	0.9	1737	0.7	3816	1.1	13386	1.6	1616	1.5	6393	1.0
ZR/EGFR (4-OHT + EGF) 0 μ M	2045	0.8	3685	0.8	3096	3.0	15398	1.5	2049	0.8	3576	1.0	12161	1.4	8392	7.5	5591	0.9
ZR/EGFR (4-OHT + EGF) 0.01 μ M	1899	0.8	3681	0.8	3502	3.4	13575	1.3	1667	0.6	3715	1.0	12557	1.5	7669	6.9	5890	0.9
ZR/EGFR (4-OHT + EGF) 0.1 μ M	1832	0.8	3948	0.9	2925	2.8	14087	1.3	1957	0.7	3402	1.0	12734	1.5	6694	6.0	4601	0.7

Sample Name	NFKBIA		IRS1		KIT (Y719)		KIT (Y721)		MARCKS		MEK1/2		Met Y1234-1235		MTOR (S2448)		MTOR (S2481)	
	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	9256	1.0	4798	1.0	17659	1.0	3100	1.0	5773	1.0	8071	1.0	7824	1.0	4117	1.0	6755	1.0
ZR/vector (E2) 0.01 μ M	9740	1.1	7130	1.5	20764	1.2	3608	1.2	5670	1.0	10700	1.3	9414	1.2	5004	1.2	7848	1.2
ZR/vector (E2) 0.1 μ M	10199	1.1	4750	1.0	19477	1.1	3391	1.1	5541	1.0	9063	1.1	8375	1.1	4012	1.0	7180	1.1
ZR/BCAR4 (E2) 0 μ M	10883	1.2	6877	1.4	20496	1.2	4689	1.5	7428	1.3	12746	1.6	11081	1.4	8217	2.0	13589	2.0
ZR/BCAR4 (E2) 0.01 μ M	7616	0.8	4514	0.9	17998	1.0	3456	1.1	6161	1.1	8578	1.1	11476	1.5	3374	0.8	5802	0.9
ZR/BCAR4 (E2) 0.1 μ M	8613	0.9	4949	1.0	17624	1.0	4036	1.3	6628	1.1	8417	1.0	10786	1.4	4230	1.0	6741	1.0
ZR/BCAR4 (4-OHT) 0 μ M	6960	0.8	3548	0.7	18657	1.1	4487	1.4	4601	0.8	11897	1.5	13739	1.8	9711	2.4	16269	2.4
ZR/BCAR4 (4-OHT) 0.01 μ M	7465	0.8	3996	0.8	19341	1.1	4774	1.5	4890	0.8	11719	1.5	12746	1.6	10239	2.5	20723	3.1
ZR/BCAR4 (4-OHT) 0.1 μ M	7624	0.8	3996	0.8	18490	1.0	3917	1.3	4564	0.8	11237	1.4	12862	1.6	10711	2.6	21807	3.2
ZR/BCAR3 (E2) 0 μ M	8639	0.9	4072	0.8	18398	1.0	3540	1.1	6355	1.1	11226	1.4	12797	1.6	6100	1.5	8300	1.2
ZR/BCAR3 (E2) 0.01 μ M	8209	0.9	3882	0.8	19226	1.1	3526	1.1	6027	1.0	9997	1.2	11533	1.5	5394	1.3	7165	1.1
ZR/BCAR3 (E2) 0.1 μ M	7465	0.8	3226	0.7	15772	0.9	3255	1.1	4032	0.7	9433	1.2	11533	1.5	6217	1.5	7824	1.2
ZR/BCAR3 (4-OHT) 0 μ M	7935	0.9	4077	0.8	20292	1.1	3670	1.2	5329	0.9	13030	1.6	15154	1.9	9691	2.4	16916	2.5
ZR/BCAR3 (4-OHT) 0.01 μ M	7130	0.8	3121	0.7	16731	0.9	3484	1.1	4117	0.7	12557	1.6	14516	1.9	9481	2.3	16043	2.4
ZR/BCAR3 (4-OHT) 0.1 μ M	7887	0.9	3544	0.7	18270	1.0	3388	1.1	4000	0.7	12247	1.5	14662	1.9	10808	2.6	19187	2.8
ZR/EGFR (E2) 0 μ M	7864	0.8	4959	1.0	17854	1.0	3601	1.2	4861	0.8	11193	1.4	13891	1.8	5670	1.4	8578	1.3
ZR/EGFR (E2) 0.01 μ M	7801	0.8	4226	0.9	16498	0.9	3605	1.2	4880	0.8	10067	1.2	12113	1.5	4474	1.1	6708	1.0
ZR/EGFR (E2) 0.1 μ M	8267	0.9	5029	1.0	17962	1.0	3729	1.2	5614	1.0	11026	1.4	12569	1.6	4939	1.2	6601	1.0
ZR/EGFR (4-OHT + EGF) 0 μ M	7458	0.8	5608	1.2	17413	1.0	3388	1.1	3759	0.7	13919	1.7	15788	2.0	11026	2.7	14721	2.2
ZR/EGFR (4-OHT + EGF) 0.01 μ M	7692	0.8	5659	1.2	18288	1.0	3663	1.2	4256	0.7	13575	1.7	15321	2.0	9136	2.2	12333	1.8
ZR/EGFR (4-OHT + EGF) 0.1 μ M	6905	0.7	5193	1.1	17536	1.0	3412	1.1	3689	0.6	12557	1.6	14618	1.9	8613	2.1	12161	1.8

Sample Name	NFKB		P38		P70s6k		p90		PKAC		PKCA		PKCD		PKCZ-I		PRAS40	
	AU	R	AU	R	AU	R		R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μM	4060	1.0	5564	1.0	2573	1.0	3498	1.0	3790	1.0	5105	1.0	2357	1.0	19341	1.0	10219	1.0
ZR/vector (E2) 0.01 μM	6273	1.5	5519	1.0	3090	1.2	4717	1.3	4032	1.1	5808	1.1	1474	0.6	20070	1.0	10499	1.0
ZR/vector (E2) 0.1 μM	4407	1.1	5405	1.0	3035	1.2	3797	1.1	5105	1.3	5508	1.1	1772	0.8	21960	1.1	9701	0.9
ZR/BCAR4 (E2) 0 μM	6003	1.5	9339	1.7	4514	1.8	3249	0.9	4871	1.3	6368	1.2	1017	0.4	16236	0.8	22026	2.2
ZR/BCAR4 (E2) 0.01 μM	3502	0.9	5745	1.0	2428	0.9	3576	1.0	2298	0.6	8682	1.7	3419	1.5	22471	1.2	12849	1.3
ZR/BCAR4 (E2) 0.1 μM	3756	0.9	6953	1.2	3191	1.2	4438	1.3	3232	0.9	8392	1.6	1951	0.8	20973	1.1	21015	2.1
ZR/BCAR4 (4-OHT) 0 μM	1828	0.5	4871	0.9	3470	1.3	2280	0.7	1128	0.3	3729	0.7	2045	0.9	13069	0.7	22925	2.2
ZR/BCAR4 (4-OHT) 0.01 μM	2022	0.5	4974	0.9	3851	1.5	2615	0.7	1028	0.3	3456	0.7	2226	0.9	12952	0.7	21655	2.1
ZR/BCAR4 (4-OHT) 0.1 μM	1901	0.5	4866	0.9	3670	1.4	2473	0.7	1175	0.3	3334	0.7	2322	1.0	12683	0.7	19497	1.9
ZR/BCAR3 (E2) 0 μM	3778	0.9	5716	1.0	3408	1.3	3767	1.1	2827	0.7	6905	1.4	2333	1.0	22925	1.2	21873	2.1
ZR/BCAR3 (E2) 0.01 μM	4056	1.0	6355	1.1	3255	1.3	3685	1.1	2853	0.8	6768	1.3	2264	1.0	21483	1.1	20374	2.0
ZR/BCAR3 (E2) 0.1 μM	1933	0.5	4180	0.8	3150	1.2	2548	0.7	2016	0.5	5949	1.2	1735	0.7	17018	0.9	17854	1.7
ZR/BCAR3 (4-OHT) 0 μM	2431	0.6	6728	1.2	3477	1.4	3038	0.9	1711	0.5	4333	0.8	2305	1.0	16059	0.8	23624	2.3
ZR/BCAR3 (4-OHT) 0.01 μM	1652	0.4	4765	0.9	3184	1.2	1926	0.6	1198	0.3	3996	0.8	1863	0.8	12978	0.7	20090	2.0
ZR/BCAR3 (4-OHT) 0.1 μM	2000	0.5	5448	1.0	3304	1.3	2217	0.6	1494	0.4	3737	0.7	2180	0.9	13602	0.7	21786	2.1
ZR/EGFR (E2) 0 μM	2649	0.7	5536	1.0	3288	1.3	3752	1.1	2774	0.7	11766	2.3	2065	0.9	21829	1.1	17001	1.7
ZR/EGFR (E2) 0.01 μM	2579	0.6	5497	1.0	2724	1.1	3491	1.0	3159	0.8	11048	2.2	1806	0.8	22004	1.1	13905	1.4
ZR/EGFR (E2) 0.1 μM	2373	0.6	6173	1.1	3087	1.2	3858	1.1	2791	0.7	12308	2.4	1986	0.8	21333	1.1	13891	1.4
ZR/EGFR (4-OHT + EGF) 0 μM	1929	0.5	5245	0.9	4056	1.6	3415	1.0	1615	0.4	15154	3.0	1786	0.8	15154	0.8	11487	1.1
ZR/EGFR (4-OHT + EGF) 0.01 μM	2458	0.6	5937	1.1	3793	1.5	3245	0.9	1914	0.5	18197	3.6	1664	0.7	15615	0.8	11499	1.1
ZR/EGFR (4-OHT + EGF) 0.1 μM	1715	0.4	4827	0.9	3484	1.4	2722	0.8	1299	0.3	14958	2.9	1373	0.6	14214	0.7	11215	1.1

Sample Name	PTEN		ARAF		BRAF		CRAF		RASGRF		SAPK/JNK		SHC		DIABLO		SMAD2	
	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	1626	1.0	2785	1.0	7716	1.0	6884	1.0	8866	1.0	1200	1.0	248	1.0	26903	1.0	4656	1.0
ZR/vector (E2) 0.01 μ M	2016	1.2	3188	1.1	8787	1.1	7943	1.2	11037	1.2	1373	1.1	288	1.2	27722	1.0	5558	1.2
ZR/vector (E2) 0.1 μ M	2246	1.4	2793	1.0	8119	1.1	8392	1.2	13616	1.5	1480	1.2	328	1.3	30333	1.1	5569	1.2
ZR/BCAR4 (E2) 0 μ M	1852	1.1	3572	1.3	11510	1.5	14257	2.1	12900	1.5	1694	1.4	7037	28.3	29144	1.1	7144	1.5
ZR/BCAR4 (E2) 0.01 μ M	1751	1.1	2599	0.9	9009	1.2	6850	1.0	14472	1.6	517	0.4	241	1.0	27447	1.0	4412	0.9
ZR/BCAR4 (E2) 0.1 μ M	1691	1.0	2899	1.0	9838	1.3	8006	1.2	13481	1.5	860	0.7	839	3.4	27174	1.0	4569	1.0
ZR/BCAR4 (4-OHT) 0 μ M	1464	0.9	4346	1.6	11373	1.5	13507	2.0	16334	1.8	1607	1.3	4900	19.7	22471	0.8	6015	1.3
ZR/BCAR4 (4-OHT) 0.01 μ M	1633	1.0	4171	1.5	11968	1.6	12862	1.9	17677	2.0	1681	1.4	4703	18.9	24588	0.9	7310	1.6
ZR/BCAR4 (4-OHT) 0.1 μ M	1797	1.1	4359	1.6	10883	1.4	10960	1.6	16731	1.9	1476	1.2	1912	7.7	24101	0.9	7887	1.7
ZR/BCAR3 (E2) 0 μ M	1871	1.2	2652	1.0	9987	1.3	9769	1.4	17344	2.0	874	0.7	385	1.6	27174	1.0	5564	1.2
ZR/BCAR3 (E2) 0.01 μ M	1867	1.1	2807	1.0	8822	1.1	10239	1.5	17137	1.9	855	0.7	308	1.2	27722	1.0	4842	1.0
ZR/BCAR3 (E2) 0.1 μ M	1447	0.9	2597	0.9	8063	1.0	9740	1.4	14618	1.6	679	0.6	207	0.8	22925	0.9	4192	0.9
ZR/BCAR3 (4-OHT) 0 μ M	1841	1.1	4514	1.6	8596	1.1	13481	2.0	19092	2.2	1088	0.9	419	1.7	27722	1.0	6081	1.3
ZR/BCAR3 (4-OHT) 0.01 μ M	1510	0.9	4101	1.5	9091	1.2	10647	1.5	15963	1.8	986	0.8	384	1.5	24101	0.9	6039	1.3
ZR/BCAR3 (4-OHT) 0.1 μ M	1607	1.0	4605	1.7	9917	1.3	12939	1.9	18124	2.0	1054	0.9	394	1.6	26370	1.0	6503	1.4
ZR/EGFR (E2) 0 μ M	1698	1.0	3385	1.2	10604	1.4	13535	2.0	14214	1.6	2169	1.8	443	1.8	25848	1.0	6317	1.4
ZR/EGFR (E2) 0.01 μ M	2289	1.4	3519	1.3	9424	1.2	10615	1.5	15522	1.8	1661	1.4	276	1.1	27174	1.0	5405	1.2
ZR/EGFR (E2) 0.1 μ M	2071	1.3	3255	1.2	9036	1.2	12394	1.8	14300	1.6	1808	1.5	296	1.2	28283	1.1	5785	1.2
ZR/EGFR (4-OHT + EGF) 0 μ M	1621	1.0	5722	2.1	10764	1.4	17206	2.5	17223	1.9	1770	1.5	1169	4.7	24101	0.9	6149	1.3
ZR/EGFR (4-OHT + EGF) 0.01 μ M	1516	0.9	6668	2.4	10209	1.3	17659	2.6	17536	2.0	1746	1.5	783	3.2	24835	0.9	5890	1.3
ZR/EGFR (4-OHT + EGF) 0.1 μ M	1467	0.9	6490	2.3	10467	1.4	13535	2.0	16220	1.8	1686	1.4	810	3.3	23389	0.9	5162	1.1

Sample Name	STAT3 (S727)		STAT3 (Y705)		STAT 5		STAT6		KDR/VEGFR2	
	AU	R	AU	R	AU	R	AU	R	AU	R
ZR/vector (E2) 0 μ M	10647	1.0	2336	1.0	862	1.0	615	1.0	15139	1.0
ZR/vector (E2) 0.01 μ M	13725	1.3	2788	1.2	1001	1.2	645	1.0	18160	1.2
ZR/vector (E2) 0.1 μ M	11396	1.1	2530	1.1	921	1.1	666	1.1	17588	1.2
ZR/BCAR4 (E2) 0 μ M	13877	1.3	2836	1.2	7879	9.1	3371	5.5	22248	1.5
ZR/BCAR4 (E2) 0.01 μ M	10467	1.0	2096	0.9	1211	1.4	901	1.5	17588	1.2
ZR/BCAR4 (E2) 0.1 μ M	11026	1.0	2387	1.0	2267	2.6	1057	1.7	14988	1.0
ZR/BCAR4 (4-OHT) 0 μ M	11755	1.1	1400	0.6	8095	9.4	2654	4.3	21015	1.4
ZR/BCAR4 (4-OHT) 0.01 μ M	13386	1.3	1547	0.7	8317	9.7	2692	4.4	21699	1.4
ZR/BCAR4 (4-OHT) 0.1 μ M	11897	1.1	1570	0.7	5699	6.6	1823	3.0	22925	1.5
ZR/BCAR3 (E2) 0 μ M	13507	1.3	2411	1.0	2231	2.6	761	1.2	18732	1.2
ZR/BCAR3 (E2) 0.01 μ M	13780	1.3	2226	1.0	1713	2.0	611	1.0	17292	1.1
ZR/BCAR3 (E2) 0.1 μ M	12357	1.2	1438	0.6	1491	1.7	465	0.8	15398	1.0
ZR/BCAR3 (4-OHT) 0 μ M	11743	1.1	1533	0.7	2305	2.7	640	1.0	19871	1.3
ZR/BCAR3 (4-OHT) 0.01 μ M	11373	1.1	1163	0.5	2150	2.5	572	0.9	17872	1.2
ZR/BCAR3 (4-OHT) 0.1 μ M	12721	1.2	1310	0.6	2550	3.0	513	0.8	19910	1.3
ZR/EGFR (E2) 0 μ M	13413	1.3	1594	0.7	1577	1.8	517	0.8	15154	1.0
ZR/EGFR (E2) 0.01 μ M	11092	1.0	1620	0.7	1377	1.6	516	0.8	14647	1.0
ZR/EGFR (E2) 0.1 μ M	11059	1.0	1734	0.7	1258	1.5	456	0.7	13712	0.9
ZR/EGFR (4-OHT + EGF) 0 μ M	19990	1.9	1377	0.6	1955	2.3	771	1.3	18920	1.2
ZR/EGFR (4-OHT + EGF) 0.01 μ M	18142	1.7	1268	0.5	1513	1.8	585	1.0	16059	1.1
ZR/EGFR (4-OHT + EGF) 0.1 μ M	17944	1.7	1177	0.5	1711	2.0	636	1.0	16831	1.1

Supplementary table 3

IC₅₀ values determined for different chemotherapeutics.

Cells cultured in medium containing estradiol (E) or 4-hydroxytamoxifen (T) and increasing concentrations of the drugs; Doxorubicin (Dox); ifosfamide (I-Fos); 5-fluorouracil (5-FU); methotrexate (MTX) and paclitaxel. A WST-1 proliferation assay was performed after 5 days.

IC₅₀ values determined by the software program Phoenix WinNonLin 6.1 as described in materials and methods.

IC₅₀ values determined in two independent experiments are presented. ND = not determined

	Dox (nM)		I-Fos (µM)		5-FU (nM)		MTX (nM)		Taxol (nM)	
	E	T	E	T	E	T	E	T	E	T
ZR/vector	16 - 20	ND	256 - 286	ND	261 - 623	ND	10 - 21	ND	3.2 - 4.2	ND
ZR/BCAR4	44 - 55	15 - 31	299 - 396	235 - 356	358 - 673	314 - 2506	11 - 14	20 - 23	2.5 - 3.3	2.5 - 3.2
ZR/BCAR1	165 - 174	102 - 162	309 - 316	165 - 175	133 - 466	598 - 673	11 - 13	23 - 25	3.1 - 4.1	2.9 - 3.8
ZR/BCAR3	15 - 39	14 - 24	227 - 283	184 - 255	257 - 331	446 - 913	10 - 11	16 - 24	2.5 - 3.7	2.5 - 3.6
ZR/EGFR	174 - 263	372 - 442	334 - 364	614 - 692	1124 - 2905	1816 - 3392	13 - 35	10 - 42	4.3 - 3.5	3.7 - 7.6

Supplementary Table 4

Associations of combined mRNA levels of *BCAR4* and *ERBB2* in primary breast tumors with metastasis-free survival and overall survival.

MFS	Univariate analysis				Multivariate analysis		
	No.	HR	95% CI	P	HR	95% CI	P
<i>ERBB2</i>							
High vs Low	69/428	1.43	1.00-2.05	.049	1.36	.93-1.98	.110
<i>BCAR4</i>							
Pos vs Neg	115/382	1.39	1.01 - 1.90	.041	1.40	1.02 - 1.93	.038
Combined addition							
<i>BCAR4</i> neg / <i>ERBB2</i> low	334	1			1		
<i>BCAR4</i> pos / <i>ERBB2</i> low	94	1.33	.93 - 1.91	.12	1.35	.94 - 1.95	.100
<i>BCAR4</i> neg / <i>ERBB2</i> high	48	1.35	.87 - 2.10	.18	1.28	.81 - 2.03	.290
<i>BCAR4</i> pos / <i>ERBB2</i> high	21	2.01	1.13 - 3.56	.017	1.95	1.08 - 3.50	.026
OS							
<i>ERBB2</i>							
High vs Low	69/428	1.48	1.03 - 2.11	.032	1.48	1.01 - 2.15	.044
<i>BCAR4</i>							
Positive vs Negative	115/382	1.55	1.13 - 2.11	.006	1.58	1.16 - 2.17	.004
Combined addition							
<i>BCAR4</i> neg / <i>ERBB2</i> low	334	1			1		
<i>BCAR4</i> pos / <i>ERBB2</i> low	94	1.44	1.00 - 2.06	.047	1.54	1.07 - 2.21	.021
<i>BCAR4</i> neg / <i>ERBB2</i> high	48	1.32	.84 - 2.08	.220	1.40	.87 - 2.25	.170
<i>BCAR4</i> pos / <i>ERBB2</i> high	21	2.41	1.40 - 4.14	.001	2.25	1.29 - 3.91	.004

To determine a possible independent relationship of the genes studied with MFS and OS, Cox multivariate regression analyses were performed, including the base model comprising the traditional prognostic factors: age, menopausal status, tumor size, grade, and *ESR1* and *PGR* mRNA levels. Abbreviations: MFS = metastases-free survival, OS = overall survival, HR = hazard ratio, CI = confidence interval, neg = negative, pos = positive.

Supplementary Table 5. Clinicopathological and biological factors of ER α -positive metastatic breast cancers^a

Clinicopathological factors	No. of patients ^b
Menopausal status ^c	
premenopausal	70
postmenopausal	223
Age ^c (years)	
≤ 55	107
56-70	109
> 70	77
Tumor size	
≤ 2 cm	78
> 2 - ≤ 5 cm	169
> 5 cm + pT4	38
Tumor grade	
good/moderate	39
unknown	94
poor	160
Histological type	
IDC	163
ILC	28
DCIS + IDC	24
Nodal status	
N0	115
N1-3	79
N > 3	86
DSR	
LRR	31
bone	150
viscera	112
DFI	
≤ 1 yr	70
> 1 -3 yr	125
> 3 yr	98
<i>BCAR4</i> mRNA status	
positive	78
negative	215
<i>ERBB2</i> mRNA status	
positive	37
negative	256

^a) 293 Patients with advanced metastatic disease and primary tumors positive for ER α protein were included in this series.

^b) because of others and unknown, numbers not always add up to 293

^c) age at start of first-line therapy for recurrent disease