

Supplemental Tables 1-5
Breast Cancer Research and Treatment

**Patient-derived luminal subtype breast cancer xenografts contain common and unique estrogen
receptor dependent gene expression signatures**

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Supplementary Table 1. Ki67 proliferation scores in patient tumor xenografts.

Tumor line	Hormone	Tumor 1	Tumor 2	Tumor 3	average
PE4	E	31 ^a	42		36.5
AS9	E	40	45		42.5
PT12	E	42	46	44	44
PT12	E+Tam	13	15	23	17
PT12	EWD	12	9		10.5
PT15	E	53	50	49	50.7
PT15	E+Tam	46	50	46	47.3
PT16	E	32	41		36.5
PT18	none	73	63		68
PT18 patient	UNK	65			
control ^b	none	49			

^aMeasured by immunohistochemistry for Ki67 followed by Ventana Image Analysis (Vias) on sections from 2-3 independent tumors.

^bHuman lymphoma cell line HL60.

Supplementary Table 2. Genes that were significantly up- or downregulated by estrogens in patient derived breast cancer xenografts PE4 and PT12 (p<0.05, >1.5 fold change).

Genes upregulated by estrogen in PE4 and PT12

Gene Symbol	Gene Assignment	PE4 (E vs. placebo)		PT12 (E vs. placebo)		MCF7 ^a (E 24h vs. vehicle)		MCF7 ^b (E 48h vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change	p value	fold change
AHNAK2	AHNAK nucleoprotein 2	0.0036	1.6981	0.0099	2.0111				
ANXA1	annexin A1	0.0115	2.7556	0.0000	3.0376				
ATP11A	ATPase, class VI, type 11A	0.0155	1.6429	0.0215	1.5138				
B4GALT1	UDP-Gal:betaGlcNAc beta 1,4- galactosyltransferase, poly	0.0002	2.5895	0.0408	1.5276				
C3orf57	chromosome 3 open reading frame 57	0.0452	1.7098	0.0016	2.7336				
CADM2	cell adhesion molecule 2	0.0046	2.7176	0.0313	3.3135				
CAPN9	calpain 9	0.0112	1.6174	0.0014	2.7728				
CARS2	cysteinyl-tRNA synthetase 2, mitochondrial (putative)	0.0022	1.7148	0.0209	1.7005				
DPY19L1^c	dpy-19-like 1 (C. elegans)	0.0112	1.5408	0.0070	1.5190			0.0275	2.1668
DSP	desmoplakin	0.0012	2.0430	0.0074	1.5381				
FARP1	FERM, RhoGEF (ARHGEF) and pleckstrin domain protein 1 (cho	0.0008	2.0351	0.0136	1.5166				
FREM2	FRAS1 related extracellular matrix protein 2	0.0008	2.1527	0.0393	1.9321				
FUS	fused in sarcoma	0.0008	1.5228	0.0091	1.9025				
GALNT4	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylga	0.0012	1.8105	0.0002	2.0196				
GREB1	growth regulation by estrogen in breast cancer 1	0.0383	1.9012	0.0104	6.9974	0.0002	7.5601	0.0008	7.5372
GRIK3	glutamate receptor, ionotropic, kainate 3	0.0012	4.4863	0.0185	1.7028				
H2AFY	H2A histone family, member Y	0.0009	1.6436	0.0059	1.5404				
HEY2	hairly/enhancer-of-split related with YRPW motif 2	0.0011	1.9823	0.0005	1.9249				
KLF6	Kruppel-like factor 6	0.0002	1.5083	0.0099	2.2360				
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	0.0025	1.9396	0.0170	1.7119	0.0254	1.8330	0.0008	3.4208
LRRFIP1	leucine rich repeat (in FLII) interacting protein 1	0.0139	1.5696	0.0217	1.6068				
MAML3	mastermind-like 3 (Drosophila)	0.0019	3.3137	0.0010	1.5862				
MID1	midline 1 (Opitz/BBB syndrome)	0.0046	2.0120	0.0371	1.7909				
MRPS25	mitochondrial ribosomal protein S25	0.0025	1.5556	0.0002	2.3402				
NOS1AP	nitric oxide synthase 1 (neuronal) adaptor protein	0.0208	1.5544	0.0028	1.9081	0.0011	1.5193		
PDIA5	protein disulfide isomerase family A, member 5	0.0022	1.7036	0.0010	2.1393				
PREX1	phosphatidylinositol-3,4,5-trisphosphate-dependent Rac exc	0.0103	2.8094	0.0440	1.6803				
RUNX1	runt-related transcription factor 1	0.0064	1.7601	0.0157	1.8049				
S100A14	S100 calcium binding protein A14	0.0035	1.7290	0.0183	1.6818				
SLC6A6	solute carrier family 6 (neurotransmitter transporter, ta	0.0057	1.7562	0.0020	2.9840				
SLC6A8	solute carrier family 6 (neurotransmitter transporter, cr	0.0274	1.5903	0.0251	1.6146				
SNHG12	small nucleolar RNA host gene 12 (non-protein coding)	0.0029	1.6856	0.0005	1.8781				
SYTL5	synaptotagmin-like 5	0.0147	1.7372	0.0002	3.4537				
TPPP3	tubulin polymerization-promoting protein family member 3	0.0002	1.8348	0.0318	1.5235				
TRIM52	tripartite motif-containing 52	0.0445	1.5747	0.0011	1.6075				
TTC39A	tetratricopeptide repeat domain 39A	0.0084	1.5419	0.0220	1.5003				

Genes downregulated by estrogen in PE4 and PT12

Gene Symbol	Gene Assignment	PE4 (E vs. placebo)		PT12 (E vs. placebo)		MCF7 ^a (E 24h vs. vehicle)		MCF7 ^b (E 48h vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change	p value	fold change
ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	0.0226	-1.7600	0.0045	-1.9298	0.0003	-2.2527	0.0000	-4.0993
ACADSB	acyl-CoA dehydrogenase, short/branched chain	0.0309	-2.4217	0.0443	-1.7963				

APOD	apolipoprotein D	0.0038	-2.5756	0.0485	-3.3223			0.0038	-5.0089
C5orf42	chromosome 5 open reading frame 42	0.0197	-1.9759	0.0200	-1.6030				
CCDC126	coiled-coil domain containing 126	0.0221	-2.0062	0.0025	-1.5580				
CD302	CD302 molecule	0.0066	-2.2678	0.0007	-2.0318				
CLU	clusterin	0.0084	-2.0058	0.0442	-1.5035	0.0024	-2.3246	0.0000	-3.6198
COLEC12	collectin sub-family member 12	0.0240	-1.5462	0.0031	-2.2792				
COX17	COX17 cytochrome c oxidase assembly homolog (S. cerevisiae)	0.0031	-1.7100	0.0017	-1.5104				
FAM102B	family with sequence similarity 102, member B	0.0161	-1.7885	0.0001	-2.0020				
FAM173B	family with sequence similarity 173, member B	0.0359	-1.6472	0.0441	-1.6206				
FMO5	flavin containing monooxygenase 5	0.0253	-2.5699	0.0177	-1.6480	0.0005	-3.3621		
GSTM3	glutathione S-transferase mu 3 (brain)	0.0141	-2.8027	0.0176	-1.5966	0.0001	-1.7486		
HIST1H2BM	histone cluster 1, H2bm	0.0015	-3.3957	0.0039	-3.3186				
LRP2	low density lipoprotein receptor-related protein 2	0.0133	-3.1125	0.0197	-1.9299	0.0008	-5.7951		
MGAT4A	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylgluco	0.0137	-1.6825	0.0000	-4.3529			0.0013	-2.6921
MPDZ	multiple PDZ domain protein	0.0423	-1.8453	0.0057	-1.6347				
PPP1R3C	protein phosphatase 1, regulatory (inhibitor) subunit 3C	0.0043	-2.6744	0.0317	-1.9293	0.0059	-3.6949	0.0001	-2.7632
PPP4R4	protein phosphatase 4, regulatory subunit 4	0.0000	-3.9929	0.0070	-1.7419				
PRKACB	protein kinase, cAMP-dependent, catalytic, beta	0.0242	-1.7232	0.0075	-1.8311			0.0421	-1.8797
RAB30	RAB30, member RAS oncogene family	0.0039	-2.9383	0.0100	-1.7119	0.0067	-1.7377		
RARRES3	retinoic acid receptor responder (tazarotene induced) 3	0.0213	-1.9008	0.0013	-2.2876				
REEP1	receptor accessory protein 1	0.0079	-2.0093	0.0000	-1.9088				
SCUBE2	signal peptide, CUB domain, EGF-like 2	0.0178	-1.6358	0.0011	-5.8264				
SEPP1	selenoprotein P, plasma, 1	0.0436	-1.5565	0.0143	-1.7700	0.0334	-1.7901		
SEPT10	septin 10	0.0033	-1.5992	0.0450	-1.6019				
SERPINI1	serpin peptidase inhibitor, clade I (neuroserpin), m	0.0313	-2.8786	0.0046	-2.9349				
SLC30A8	solute carrier family 30 (zinc transporter), member 8	0.0004	-3.2431	0.0266	-2.0221				
SQRDL	sulfide quinone reductase-like (yeast)	0.0035	-1.6301	0.0022	-1.5919			0.0321	-1.9094
TMEM60	transmembrane protein 60	0.0038	-1.8607	0.0008	-1.5029				
TNIK	TRAF2 and NCK interacting kinase	0.0013	-1.6765	0.0040	-2.5863				
TPRG1	tumor protein p63 regulated 1	0.0123	-2.0119	0.0014	-7.9217				
TTLL7	tubulin tyrosine ligase-like family, member 7	0.0236	-2.0150	0.0290	-1.5141				
ZBTB38	zinc finger and BTB domain containing 38	0.0272	-1.6793	0.0167	-1.6927				
ZMAT1	zinc finger, matrin-type 1	0.0410	-2.0566	0.0412	-1.5995				

^adetermined by importing dataset GSE3834 into Partek Genomics Suite and cross analyzing the E regulated genes at 24h vs. vehicle with that for PE4 and PT1

^bdetermined by importing dataset GSE848 into Partek Genomics Suite and cross analyzing the E regulated genes at 48h vs vehicle with that for PE4 and PT12

^cgenes also regulated in MCF7 cells are indicated in bold

Supplemental Table 3. Genes that were significantly up- or downregulated by estrogen in xenograft PE4 and MCF7 cells

Genes upregulated by estrogen in PE4 and MCF7 cells

Gene Symbol	Gene Assignment	PE4 (E vs. placebo)		MCF7 ^a (E 24h vs. vehicle)		MCF7 ^b (E 48h vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change
CXCL12	chemokine (C-X-C motif) ligand 12	0.0058	2.8930	0.0000	7.4458	0.0031	4.1194
IGFBP5 ^c	insulin-like growth factor binding protein 5	0.0193	1.6604	0.0024	3.9857	0.0067	-1.9389
MYBL1	v-myb myeloblastosis viral oncogene homolog (avian)-lik	0.0215	1.5058	0.0096	4.9684	0.0119	4.2726
CCDC88C	coiled-coil domain containing 88C	0.0005	4.3296	0.0415	1.7125		
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	0.0004	3.5260	0.0221	2.0589		
ZNF238	zinc finger protein 238	0.0000	3.3468	0.0175	1.9864		
PITX1	paired-like homeodomain 1	0.0018	3.1263	0.0257	1.7593		
PCDH7	protocadherin 7	0.0276	2.1694	0.0028	1.9326		
BFSP2	beaded filament structural protein 2, phakinin	0.0010	1.9107	0.0037	3.5135		
IRS1	insulin receptor substrate 1	0.0315	1.8289	0.0362	1.7249		
PLCB2	phospholipase C, beta 2	0.0034	1.8287	0.0262	2.3371		
IGFBP4	insulin-like growth factor binding protein 4	0.0463	1.8268	0.0000	4.3662		
USP10	ubiquitin specific peptidase 10	0.0000	1.6138	0.0252	1.9480		
ELF1	E74-like factor 1 (ets domain transcription factor)	0.0110	1.5867	0.0004	2.1860		
CSNK2A2	casein kinase 2, alpha prime polypeptide	0.0001	1.5353	0.0018	1.9496		
DLEU1	deleted in lymphocytic leukemia 1 (non-protein coding)	0.0016	1.5327	0.0011	2.0886		
RAPGEFL1	Rap guanine nucleotide exchange factor (GEF)-like 1	0.0185	2.4652			0.0018	2.0482
TSKU	tsukushi small leucine rich proteoglycan homolog (Xenopus I	0.0204	2.4355			0.0008	2.1076
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	0.0033	1.8314			0.0009	2.1909
SCNN1B	sodium channel, nonvoltage-gated 1, beta	0.0003	1.8133			0.0075	1.6195
CA8	carbonic anhydrase VIII	0.0349	1.6258			0.0003	2.4579
TRAP1	TNF receptor-associated protein 1	0.0004	1.5939			0.0251	1.5962
GFRA1	GDNF family receptor alpha 1	0.0020	1.5199			0.0139	1.9436

Genes downregulated by estrogen in PE4 and MCF7 cells

Gene Symbol	Gene Assignment	PE4 (E vs. placebo)		MCF7 ^a (E 24h vs. vehicle)		MCF7 ^b (E 48h vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change
DEBS1	degenerative spermatocyte homolog 1, lipid desaturase (Dro	0.0000	-3.9628	0.0046	-1.7285	0.0228	-2.5707
EFEMP1	EGF-containing fibulin-like extracellular matrix protein	0.0313	-1.9897	0.0065	-2.0404	0.0211	-2.5249
PLCB1 ^c	phospholipase C, beta 1 (phosphoinositide-specific)	0.0108	-1.9417	0.0149	2.3444	0.0008	-5.1838
REEP5	receptor accessory protein 5	0.0000	-1.9168	0.0011	-1.6452	0.0435	-2.1849
ABCC3	ATP-binding cassette, sub-family C (CFTR/MRP)	0.0022	-1.8558	0.0339	-1.9521	0.0155	-1.9892
PTPRK	protein tyrosine phosphatase, receptor type, K	0.0069	-1.7284	0.0005	-1.9769	0.0064	-2.3595
ZNF217	zinc finger protein 217	0.0006	-1.7028	0.0061	-2.1675	0.0210	-2.7658
TBC1D9	TBC1 domain family, member 9 (with GRAM domain)	0.0299	-1.6818	0.0071	-1.9199	0.0031	-2.0569

PLSCR1 ^c	phospholipid scramblase 1	0.0285	-1.6447	0.0412	2.7902	0.0345	-1.7519
ARNT2	aryl-hydrocarbon receptor nuclear translocator 2	0.0030	-1.5821	0.0024	-2.4366	0.0003	-4.1029
EXT1	exostosin 1	0.0005	-1.5609	0.0078	-1.9136	0.0180	-2.2316
NCOA1 ^c	nuclear receptor coactivator 1	0.0002	-1.5329	0.0131	1.5338	0.0051	-2.1358
ATP2B1	ATPase, Ca ⁺⁺ transporting, plasma membrane 1	0.0004	-1.5315	0.0257	-1.5691	0.0321	-2.6862
AMIGO2	adhesion molecule with Ig-like domain 2	0.0022	-3.5262	0.0242	-1.9959		
ALDHB2	aldehyde dehydrogenase 3 family, member B2	0.0034	-3.4937	0.0111	-1.5166		
NELL2	NEL-like 2 (chicken)	0.0198	-3.1370	0.0001	-4.2687		
DCLK1	doublecortin-like kinase 1	0.0127	-2.9794	0.0407	-4.9398		
UGCG	UDP-glucose ceramide glucosyltransferase	0.0000	-2.8354	0.0253	-4.2542		
CTSH	cathepsin H	0.0000	-2.3196	0.0000	-2.6606		
KIAA1467	KIAA1467	0.0006	-2.0953	0.0020	-1.9651		
KCNMA1	potassium large conductance calcium-activated channel,	0.0004	-1.8757	0.0188	-1.7074		
C10orf116	chromosome 10 open reading frame 116	0.0095	-1.8651	0.0001	-3.2749		
FN1	fibronectin 1	0.0456	-1.7884	0.0393	-2.0841		
CAMK2B	calcium/calmodulin-dependent protein kinase II beta	0.0034	-1.7700	0.0284	-1.5490		
NVL	nuclear VCP-like	0.0030	-1.7397	0.0344	-1.5459		
SRGAP3	SLIT-ROBO Rho GTPase activating protein 3	0.0035	-1.6691	0.0302	-1.5608		
IER3	immediate early response 3	0.0164	-1.6672	0.0004	-3.1870		
PCSK6	proprotein convertase subtilisin/kexin type 6	0.0225	-1.5788	0.0134	-1.7592		
SLC7A8	solute carrier family 7 (amino acid transporter, L-type),	0.0212	-1.5719	0.0233	-1.5872		
KCNJ3	potassium inwardly-rectifying channel, subfamily J, member	0.0244	-6.7475			0.0252	-1.6673
MGLL	monoglyceride lipase	0.0000	-3.3468			0.0027	-1.8678
ARHGAP29	Rho GTPase activating protein 29	0.0034	-2.6087			0.0060	-2.6963
NR4A2	nuclear receptor subfamily 4, group A, member 2	0.0006	-2.3128			0.0076	-1.6484
CGA	glycoprotein hormones, alpha polypeptide	0.0005	-2.2626			0.0249	-1.5803
VTCN1	V-set domain containing T cell activation inhibitor 1	0.0020	-1.9955			0.0010	-3.6684
MYO6	myosin VI	0.0010	-1.8854			0.0170	-2.4509
FUT8	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	0.0064	-1.8565			0.0211	-2.1720
CRABP1	cellular retinoic acid binding protein 1	0.0084	-1.8465			0.0198	-1.7653
MXRA7	matrix-remodelling associated 7	0.0391	-1.7403			0.0121	-2.0274
KRT15	keratin 15	0.0003	-1.7343			0.0021	-2.7804
MFSD1	major facilitator superfamily domain containing 1	0.0160	-1.7275			0.0146	-1.8097
OSR2	odd-skipped related 2 (Drosophila)	0.0175	-1.7233			0.0055	-1.8714
PPP1R2	protein phosphatase 1, regulatory (inhibitor) subunit 2	0.0055	-1.7229			0.0094	-2.4388
CAV2	caveolin 2	0.0097	-1.7193			0.0304	-2.7613
ID2	inhibitor of DNA binding 2, dominant negative helix-loop-hel	0.0001	-1.7107			0.0136	-1.7784
SIDT1	SID1 transmembrane family, member 1	0.0001	-1.6554			0.0031	-2.0050
TBC1D8	TBC1 domain family, member 8 (with GRAM domain)	0.0059	-1.6548			0.0055	-1.7857
ATP1B1	ATPase, Na ⁺ /K ⁺ transporting, beta 1 polypeptide	0.0245	-1.6368			0.0149	-2.0095
SLC31A2	solute carrier family 31 (copper transporters), member 2	0.0057	-1.6339			0.0121	-1.6899

SPAG1	sperm associated antigen 1	0.0004	-1.6129	0.0253	-3.0819
MEGF9	multiple EGF-like-domains 9	0.0052	-1.5884	0.0046	-2.4701
CRABP2	cellular retinoic acid binding protein 2	0.0053	-1.5560	0.0039	-2.2333
RAB27B	RAB27B, member RAS oncogene family	0.0395	-1.5283	0.0120	-1.8197
OAT	ornithine aminotransferase	0.0079	-1.5159	0.0151	-2.8425
SCYL3	SCY1-like 3 (<i>S. cerevisiae</i>)	0.0216	-1.5051	0.0466	-1.6084

^adetermined by importing dataset GSE3834 into Partek Genomics Suite and cross analyzing the E regulated genes at 24h vs. vehicle with that for PE4

^bdetermined by importing dataset GSE848 into Partek Genomics Suite and cross analyzing the E regulated genes at 48h vs vehicle with that for PE4

^cregulated in opposite directions in the two MCF7 datasets

Supplemental Table 4. Genes that were significantly up- or downregulated by estrogen in xenograft PT12 and MCF7 cells**Genes upregulated by estrogen in PT12 and MCF7 cells**

Gene Symbol	Gene Assignment	PT12(E vs. placebo)		MCF7 ^a (E vs. vehicle)		MCF7 ^b (E vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change
IGF1R	insulin-like growth factor 1 receptor	0.0076	3.4567	0.0075	1.7710	0.0341	1.6409
NPY1R	neuropeptide Y receptor Y1	0.0061	3.4276	0.0483	2.9539	0.0022	1.9165
KRT7 ^c	keratin 7	0.0129	3.1712	0.0454	3.0057	0.0006	-2.7195
AREG	amphiregulin	0.0064	3.0465	0.0008	6.5557	0.0048	4.1297
PRSS23	protease, serine, 23	0.0019	2.2374	0.0007	4.5111	0.0039	1.9276
SAT1 ^c	spermidine/spermine N1-acetyltransferase 1	0.0038	2.0651	0.0442	2.1351	0.0056	-3.8998
PLS1 ^c	plastin 1	0.0074	1.7504	0.0206	1.8988	0.0329	-1.9894
CELSR2	cadherin, EGF LAG seven-pass G-type receptor 2 (flamingo)	0.0463	1.7188	0.0024	1.8936	0.0029	2.6628
KYNU ^c	kynureninase (L-kynurenine hydrolase)	0.0446	1.6097	0.0381	2.9128	0.0213	-2.0076
CENPA	centromere protein A	0.0019	1.6060	0.0038	3.1816	0.0020	3.9563
OIP5	Opa interacting protein 5	0.0460	1.5767	0.0269	2.3099	0.0227	2.2574
RAD54L	RAD54-like (<i>S. cerevisiae</i>)	0.0096	1.5642	0.0100	1.6375	0.0100	1.5334
KIFC1	kinesin family member C1	0.0101	1.5256	0.0258	1.6815	0.0002	1.7886
RAB31	RAB31, member RAS oncogene family	0.0004	7.0704	0.0000	4.0560		
MPPED2	metallophosphoesterase domain containing 2	0.0004	5.8904	0.0002	3.0312		
FBXO9	F-box protein 9	0.0027	3.1880	0.0457	1.6081		
TPBG	trophoblast glycoprotein	0.0240	3.0670	0.0000	2.1494		
RASGRP1	RAS guanyl releasing protein 1 (calcium and DAG-regulate	0.0161	2.7318	0.0351	3.3124		
C1orf63	chromosome 1 open reading frame 63	0.0001	2.5259	0.0126	1.7612		
RHOBTB3	Rho-related BTB domain containing 3	0.0008	2.4089	0.0013	3.3539		
TMPO	thymopoietin	0.0309	2.1942	0.0178	1.8385		
CDK2AP1	cyclin-dependent kinase 2 associated protein 1	0.0191	2.1929	0.0299	1.5625		
SRSF2	serine/arginine-rich splicing factor 2	0.0143	2.1454	0.0289	1.7620		
WEE1	WEE1 homolog (<i>S. pombe</i>)	0.0158	2.0619	0.0115	2.5225		
DDB2	damage-specific DNA binding protein 2, 48kDa	0.0146	2.0155	0.0001	2.2095		
SLC39A8	solute carrier family 39 (zinc transporter), member 8	0.0069	2.0146	0.0013	2.5558		
PLP1	proteolipid protein 1	0.0050	1.9880	0.0487	2.4113		
NRXN3	neurexin 3	0.0143	1.9128	0.0236	1.5926		
AP1S2	adaptor-related protein complex 1, sigma 2 subunit	0.0071	1.8694	0.0224	2.2578		
PFKP	phosphofructokinase, platelet	0.0329	1.8661	0.0017	1.5328		
SMG1	SMG1 homolog, phosphatidylinositol 3-kinase-related k	0.0008	1.8585	0.0068	2.7722		
HOXC6	homeobox C6	0.0092	1.8327	0.0000	2.5005		
CDK2	cyclin-dependent kinase 2	0.0289	1.8165	0.0402	1.5264		
COQ2	coenzyme Q2 homolog, prenyltransferase (yeast)	0.0058	1.8137	0.0002	2.2270		
SSFA2	sperm specific antigen 2	0.0004	1.7891	0.0402	1.7464		
SRSF1	serine/arginine-rich splicing factor 1	0.0002	1.7223	0.0242	1.5694		
BCL6	B-cell CLL/lymphoma 6	0.0015	1.7168	0.0018	1.5238		
MTDH	metadherin	0.0267	1.7103	0.0131	1.8038		
ZWINT	ZW10 interactor	0.0081	1.7099	0.0132	1.6426		
NRIP1	nuclear receptor interacting protein 1	0.0085	1.6740	0.0003	4.1552		
CTDSPL	CTD (carboxy-terminal domain, RNA polymerase II, polyp	0.0145	1.6521	0.0016	1.5558		

MALT1	mucosa associated lymphoid tissue lymphoma translocation g	0.0057	1.6410	0.0429	1.6267		
SLC22A5	solute carrier family 22 (organic cation/carnitine trans	0.0068	1.6385	0.0000	3.1855		
GINS1	GINS complex subunit 1 (Psf1 homolog)	0.0239	1.6207	0.0358	1.7772		
PRPS2	phosphoribosyl pyrophosphate synthetase 2	0.0149	1.5924	0.0213	1.5150		
CDR2	cerebellar degeneration-related protein 2, 62kDa	0.0086	1.5839	0.0339	1.9183		
CACNB1	calcium channel, voltage-dependent, beta 1 subunit	0.0348	1.5816	0.0363	1.8256		
PGRMC1	progesterone receptor membrane component 1	0.0096	1.5599	0.0169	1.7063		
YES1	v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1	0.0161	1.5476	0.0145	1.7512		
WHSC1	Wolf-Hirschhorn syndrome candidate 1	0.0164	1.5407	0.0328	1.6716		
TIPARP	TCDD-inducible poly(ADP-ribose) polymerase	0.0044	1.5223	0.0018	2.2917		
RAP2A	RAP2A, member of RAS oncogene family	0.0153	1.5095	0.0005	3.7529		
DDX23	DEAD (Asp-Glu-Ala-Asp) box polypeptide 23	0.0207	1.5024	0.0018	1.5038		
SERPINA3	serpin peptidase inhibitor, clade A (alpha-1 antiprotei	0.0181	3.8425			0.0003	2.7709
SHMT2	serine hydroxymethyltransferase 2 (mitochondrial)	0.0339	2.1723			0.0001	1.9781
KIF22	kinesin family member 22	0.0206	2.1553			0.0002	1.5438
FLNB	filamin B, beta	0.0156	2.0853			0.0125	1.8514
ABHD2	abhydrolase domain containing 2	0.0005	2.0659			0.0386	1.5450
IL17RB	interleukin 17 receptor B	0.0139	2.0542			0.0409	1.6970
SLC1A4	solute carrier family 1 (glutamate/neutral amino acid tra	0.0018	1.8706			0.0461	1.5196
THOC6	THO complex 6 homolog (Drosophila)	0.0462	1.8653			0.0185	1.9817
BCS1L	BCS1-like (S. cerevisiae)	0.0039	1.7203			0.0141	1.5686
BOP1	block of proliferation 1	0.0384	1.6929			0.0414	1.6355
HJURP	Holliday junction recognition protein	0.0037	1.6210			0.0049	1.5442
IMP4	IMP4, U3 small nucleolar ribonucleoprotein, homolog (yeast)	0.0406	1.6186			0.0331	1.5445
SLC16A1	solute carrier family 16, member 1 (monocarboxylic ac	0.0288	1.5996			0.0348	1.6135
TIMELESS	timeless homolog (Drosophila)	0.0194	1.5934			0.0071	1.7971
RET	ret proto-oncogene	0.0415	1.5668			0.0110	2.3941

Genes downregulated by estrogen in PT12 and MCF7 cells

Gene Symbol	Gene Assignment	PE4 (E vs. placebo)		MCF7 ^a (E vs. vehicle)		MCF7 ^b (E vs. vehicle)	
		p value	fold change	p value	fold change	p value	fold change
IGFBP5 ^c	insulin-like growth factor binding protein 5 // 2q33-q36	0.0000	-6.9118	0.0024	3.9857	0.0067	-1.9389
NMI ^c	N-myc (and STAT) interactor	0.0057	-2.5659	0.0283	2.1350	0.0181	-2.1158
MT1G ^c	metallothionein 1G	0.0037	-2.2627	0.0081	-2.5612	0.0145	1.5222
IL1R1	interleukin 1 receptor, type I	0.0097	-1.9653	0.0000	-20.6679	0.0041	-2.7086
RAB9A	RAB9A, member RAS oncogene family	0.0062	-1.7558	0.0011	-2.2166	0.0365	-2.0419
TRAF5 ^c	TNF receptor-associated factor 5 // 1q32 // 7188 /// NM_00	0.0395	-1.6967	0.0484	1.5783	0.0112	-2.5905
S100A10	S100 calcium binding protein A10	0.0054	-1.5833	0.0025	-1.5332	0.0008	-1.6989
RWDD2A	RWD domain containing 2A	0.0461	-1.5649	0.0115	-2.0835	0.0068	-2.4669
HOPX	HOP homeobox	0.0019	-1.5202	0.0453	-3.9143	0.0108	-2.9189
PVALB	parvalbumin	0.0011	-14.7145	0.0000	-7.4743		
MT1A	metallothionein 1A	0.0011	-5.4612	0.0002	-2.3006		
INSIG2	insulin induced gene 2	0.0274	-2.7457	0.0002	-2.9188		
STC1	stanniocalcin 1	0.0002	-2.3420	0.0078	-2.1214		
PHEX	phosphate regulating endopeptidase homolog, X-linked	0.0178	-2.3232	0.0377	-2.1489		

CLUAP1	clusterin associated protein 1 // 16p13.3 // 23059 /// NM	0.0106	-2.0227	0.0318	-1.5119		
DBI	diazepam binding inhibitor (GABA receptor modulator, acyl-Co	0.0058	-1.9828	0.0000	-1.6608		
UPK1A	uroplakin 1A	0.0018	-1.9266	0.0084	-2.4339		
YIPF1	Yip1 domain family, member 1 // 1p33-p32.1 // 54432 /// NR	0.0158	-1.8580	0.0039	-1.6453		
CYP2J2	cytochrome P450, family 2, subfamily J, polypeptide 2 //	0.0305	-1.7731	0.0172	-1.5195		
PRPS1	phosphoribosyl pyrophosphate synthetase 1	0.0287	-1.7371	0.0042	-1.9052		
ACPP	acid phosphatase, prostate // 3q21-q23 // 55 /// NM_0011341	0.0422	-1.6136	0.0424	-1.5283		
ACO1	aconitase 1, soluble // 9p22-q32 9p21.1 // 48 /// ENST00000	0.0088	-1.6021	0.0003	-1.6105		
PLA2R1	phospholipase A2 receptor 1, 180kDa	0.0357	-1.6000	0.0427	-2.1477		
ATP6V1E1	ATPase, H+ transporting, lysosomal 31kDa, V1 subunit E1	0.0067	-1.5935	0.0025	-1.5163		
BLNK	B-cell linker	0.0364	-1.5877	0.0097	-2.3103		
HLTF	helicase-like transcription factor // 3q25.1-q26.1 // 6596	0.0284	-1.5669	0.0173	-1.7328		
AKAP5	A kinase (PRKA) anchor protein 5	0.0197	-1.5463	0.0026	-3.1879		
BRE	brain and reproductive organ-expressed (TNFRSF1A modulator)	0.0009	-1.5180	0.0002	-1.9391		
DYNLRB1	dynein, light chain, roadblock-type 1	0.0003	-2.5772			0.0474	-1.5062
HEBP1	heme binding protein 1	0.0014	-2.4174			0.0341	-1.8391
SAP18	Sin3A-associated protein, 18kDa	0.0002	-2.2056			0.0252	-1.6333
NBEA	neurobeachin	0.0207	-2.1695			0.0151	-3.7677
GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2	0.0033	-2.1458			0.0268	-1.5191
NPC2	Niemann-Pick disease, type C2	0.0062	-2.0671			0.0301	-1.6105
SGMS1	sphingomyelin synthase 1	0.0278	-1.9939			0.0359	-2.1285
KIAA0196	KIAA0196	0.0044	-1.9848			0.0399	-1.6328
C3orf14	chromosome 3 open reading frame 14	0.0326	-1.9295			0.0442	-1.7383
S100A11	S100 calcium binding protein A11	0.0014	-1.9045			0.0002	-1.6046
HIST1H2BK	HIST1H2BK // histone cluster 1, H2bk	0.0029	-1.8142			0.0045	-1.9491
UBR7	ubiquitin protein ligase E3 component n-recognin 7 (putativ	0.0372	-1.7779			0.0098	-1.6325
C6orf97	chromosome 6 open reading frame 97 // 6q25.1 // 80129 //	0.0125	-1.7209			0.0338	-2.4571
ARID5B	AT rich interactive domain 5B (MRF1-like)	0.0263	-1.7208			0.0081	-3.3378
MANSC1	MANSC domain containing 1	0.0102	-1.7087			0.0224	-1.8637
ANK3	ankyrin 3, node of Ranvier	0.0455	-1.6878			0.0058	-1.8658
LXN	latexin	0.0231	-1.6788			0.0000	-3.6474
VAMP8	vesicle-associated membrane protein 8 (endobrevin)	0.0028	-1.6467			0.0355	-3.1260
ATP5E	ATP synthase, H+ transporting, mitochondrial F1 complex	0.0023	-1.5856			0.0146	-1.5317
UBE2L6	ubiquitin-conjugating enzyme E2L 6 // 11q12 // 9246 /// N	0.0284	-1.5674			0.0065	-1.7714
DAZAP2	DAZ associated protein 2 // 12q12 // 9802 /// NM_00113626	0.0393	-1.5665			0.0320	-1.8282
MAPKSP1	MAPK scaffold protein 1	0.0320	-1.5626			0.0435	-2.5338
SH3BGRL	SH3 domain binding glutamic acid-rich protein like	0.0204	-1.5464			0.0068	-3.9116
SMARCE1	SWI/SNF related, matrix associated, actin dependent regu	0.0006	-1.5337			0.0103	-2.5699
TMBIM6	transmembrane BAX inhibitor motif containing 6	0.0082	-1.5217			0.0048	-2.1136
YPEL5	yippee-like 5 (Drosophila)	0.0097	-1.5132			0.0010	-3.7873
SKP1	S-phase kinase-associated protein 1	0.0336	-1.5122			0.0499	-1.9567
FAM3C	family with sequence similarity 3, member C // 7q31 // 104	0.0436	-1.5028			0.0347	-1.8255

^adetermined by importing dataset GSE3834 into Partek Genomics Suite and cross analyzing the E regulated genes at 24h vs. vehicle with those for PT12 E vs. placebo

^bdetermined by importing dataset GSE848 into Partek Genomics Suite and cross analyzing the E regulated genes at 48h vs. vehicle with those for PT12 E vs. placebo

^cregulated in opposite directions in the two MCF7 datasets

Supplementary Table 5. Estrogen up- and down- regulated genes in breast cancer xenograft PT12 that significantly changed in the opposite direction with both tamoxifen and EWD treatment (p<0.05, >1.5 fold).

Genes upregulated by estrogen and downregulated with E+Tam and EWD

Gene Symbol	Gene Assignment	E vs. placebo		E+Tam vs. E		EWD vs. E		MCF7 ^a (E+TOT vs. E)		MCF7 ^b (EWD vs. E)	
		p value	fold change	p value	fold change	p value	fold change	p value	fold change	p value	fold change
ABAT	4-aminobutyrate aminotransferase	0.0172	2.0946	0.0300	-1.9299	0.0267	-1.9633			0.0484	1.7393
ABCC2	ATP-binding cassette, sub-family C (CFTR/MRP), member 2	0.0000	2.8698	0.0001	-2.2119	0.0004	-2.0162	0.0149	3.4628		
BDKRB2	bradykinin receptor B2	0.0012	2.0633	0.0261	-1.5391	0.0009	-2.1290				
C10orf116	chromosome 10 open reading frame 116	0.0005	2.1093	0.0016	-1.8990	0.0005	-2.1029				
CDCA5	cell division cycle associated 5	0.0094	1.6479	0.0149	-1.5811	0.0147	-1.5829				
CHRNA5	cholinergic receptor, nicotinic, alpha 5	0.0372	1.9227	0.0351	-1.9400	0.0226	-2.0774			0.0026	2.0006
CRABP1	cellular retinoic acid binding protein 1	0.0016	3.3720	0.0044	-2.8405	0.0422	-1.9581				
EFNA5	ephrin-A5	0.0366	1.6763	0.0418	-1.6490	0.0433	-1.6421				
EGLN3	egl nine homolog 3 (C. elegans)	0.0010	7.7939	0.0302	-3.1787	0.0232	-3.4055				
FAM38B	family with sequence similarity 38, member B	0.0171	1.8279	0.0034	-2.2256	0.0047	-2.1366				
GINS1	GINS complex subunit 1 (Psf1 homolog)	0.0239	1.6207	0.0083	-1.8088	0.0158	-1.6913				
GREB1	growth regulation by estrogen in breast cancer 1	0.0104	6.9974	0.0275	-4.9644	0.0430	-4.2334	0.0148	3.2822	0.0015	5.7569
HIST1H2AB	histone cluster 1, H2ab	0.0316	1.5886	0.0179	-1.6870	0.0139	-1.7317				
HJURP	Holliday junction recognition protein	0.0037	1.6210	0.0047	-1.5935	0.0029	-1.6525				
IGF1R	insulin-like growth factor 1 receptor	0.0076	3.4567	0.0941	-2.0068	0.0212	-2.7761	0.0119	1.6848	0.0109	3.4155
LOC100127981	hypothetical protein LOC100127980	0.0111	1.8422	0.0204	-1.7201	0.0036	-2.0921				
LOC51152	melanoma antigen	0.0007	2.3226	0.0629	-1.4585	0.0022	-2.0664				
LOH3CR2A	loss of heterozygosity, 3, chromosomal region 2, gene A	0.0000	1.8499	0.0004	-1.6119	0.0013	-1.5004				
MAP3K8	mitogen-activated protein kinase kinase kinase 8	0.0013	2.4165	0.0211	-1.7389	0.0198	-1.7517				
MGAM	maltase-glucoamylase (alpha-glucosidase)	0.0001	3.1062	0.0003	-2.6268	0.0001	-2.9083				
MPPED2	metallophosphoesterase domain containing 2	0.0004	5.8904	0.0021	-4.0747	0.0062	-3.2702				
NOS1AP	nitric oxide synthase 1 (neuronal) adaptor protein	0.0028	1.9081	0.0058	-1.7782	0.0067	-1.7542				
NRIP1	nuclear receptor interacting protein 1	0.0085	1.6740	0.0091	-1.6640	0.0089	-1.6660	0.0317	1.8466	0.0264	1.7688
OTUD7A	OTU domain containing 7A	0.0044	2.1710	0.0105	-1.9528	0.0014	-2.5223				
PRSS23	protease, serine, 23	0.0019	2.2374	0.0022	-2.2070	0.0038	-2.0679	0.0005	4.9945	0.0204	2.1767
RAB31	RAB31, member RAS oncogene family	0.0004	7.0704	0.0024	-4.5410	0.0128	-3.1479				
SKA2	spindle and kinetochore associated complex subunit 2	0.0054	1.5759	0.0055	-1.5728	0.0007	-1.8521				
ST8SIA6	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransf	0.0017	5.6894	0.0264	-2.9390	0.0153	-3.3445				
STARD4	StAR-related lipid transfer (START) domain containing 4	0.0171	1.8212	0.0220	-1.7664	0.0117	-1.9041			0.0167	1.6682
TFPI2	tissue factor pathway inhibitor 2	0.0004	4.0762	0.0066	-2.5474	0.0017	-3.1801				
ZNF814	zinc finger protein 814	0.0004	2.6123	0.0175	-1.7185	0.0000	-3.6187				

Genes downregulated by estrogen and upregulated with E+Tam and EWD

Gene Symbol	Gene Assignment	E vs. placebo		E+Tam vs. E		EWD vs. E		MCF7 ^a (E+TOT vs. E)		MCF7 ^b (EWD vs. E)	
		p value	fold change	p value	fold change	p value	fold change	p value	fold change	p value	fold change
ANG	angiogenin, ribonuclease, RNase A family	0.0185	-1.8181	0.0429	1.6415	0.0431	1.6404			0.0031	-2.3793
CPB1	carboxypeptidase B1 (tissue)	0.0054	-19.8861	0.0027	27.8973	0.0284	8.8504				
DACH1	DACH1 // dachshund homolog 1 (Drosophila)	0.0004	-3.2984	0.0029	2.4684	0.0172	1.9445	0.0149	-3.3799		
ERBB4	v-erb-a erythroblastic leukemia viral oncogene homolog 4	0.0086	-3.3346	0.0054	3.6834	0.0175	2.8664				
ERP27	endoplasmic reticulum protein 27	0.0071	-3.1404	0.0104	2.9116	0.0496	2.1486				
GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2	0.0033	-2.1458	0.0008	2.5530	0.0331	1.6437				
IGFBP5	insulin-like growth factor binding protein 5	0.0000	-6.9118	0.0035	2.5456	0.0121	2.1348			0.0368	-2.4230

IL1RAPL2	interleukin 1 receptor accessory protein-like 2	0.0028	-2.1060	0.0002	2.9380	0.0052	1.9672		
INSIG2	insulin induced gene 2	0.0274	-2.7457	0.0360	2.5823	0.0144	3.1671	0.0079	-1.8177
IQGAP2	IQ motif containing GTPase activating protein 2	0.0440	-1.7199	0.0049	2.3070	0.0246	1.8600		
MT1M	metallothionein 1M	0.0025	-1.7291	0.0099	1.5501	0.0108	1.5389		
NCRNA00152	non-protein coding RNA 152	0.0001	-3.0283	0.0438	1.5511	0.0068	1.8962		
NDST4	N-deacetylase/N-sulfotransferase (heparan glucosaminyl) 4	0.0221	-1.8296	0.0229	1.8210	0.0277	1.7772		
PTN	pleiotrophin	0.0334	-1.6439	0.0176	1.7690	0.0267	1.6869		
RNF128	ring finger protein 128	0.0097	-2.1164	0.0018	2.6602	0.0074	2.1954		

^adetermined by importing dataset GSE3834 into Partek Genomics Suite and cross analyzing the E regulated genes at 24h E + 4-hydroxytamoxifen (TOT) vs. E

^bdetermined by importing dataset GSE848 into Partek Genomics Suite and cross analyzing the E regulated genes at 48h EWD vs E