

Supplementary data:

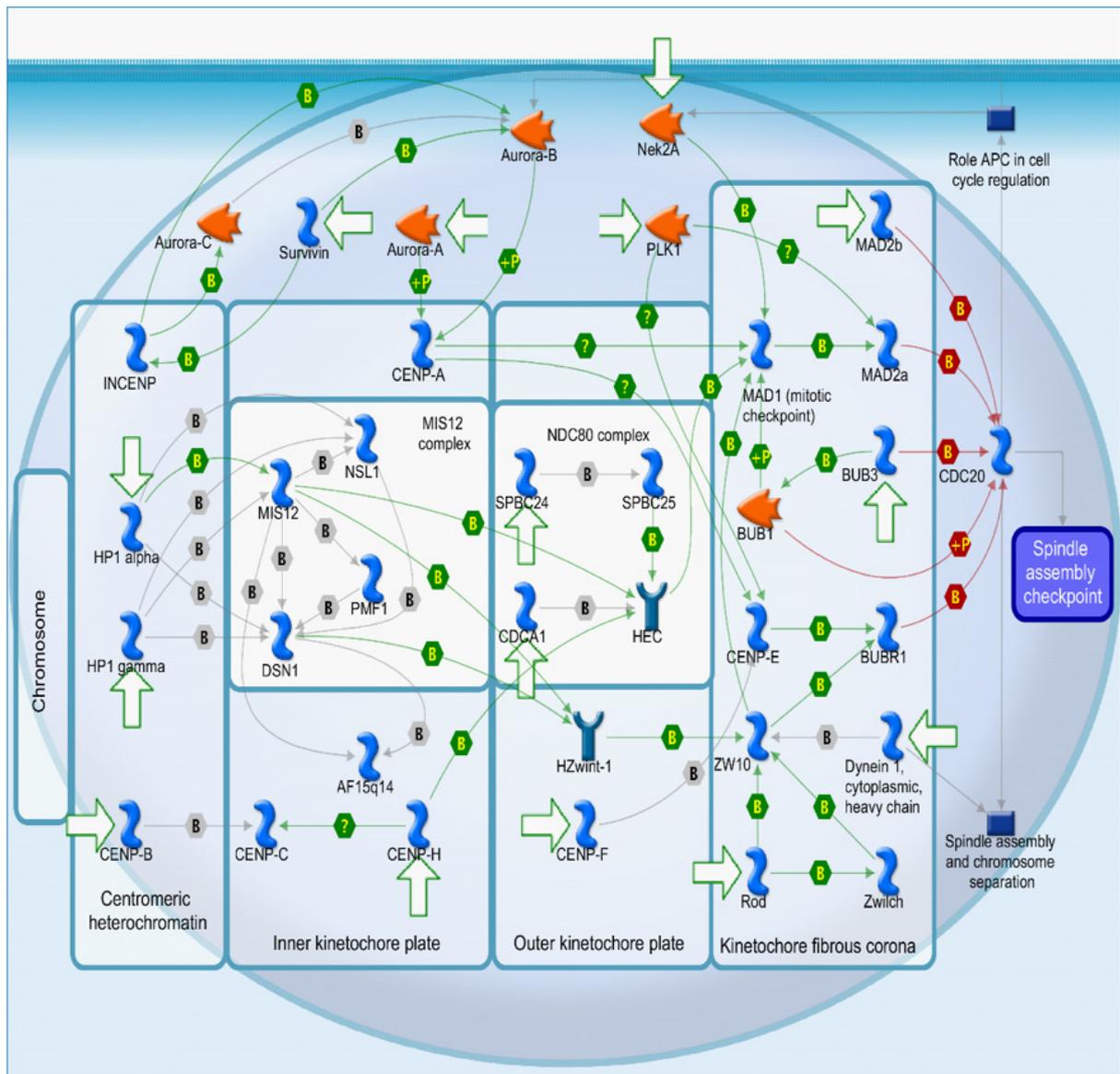


Figure S1. MetaCore pathway analysis of the coexpression gene network of pituitary tumor-transforming gene 1 (PTTG1) in breast cancer patients. Downstream pathway analyses based on the top quartile genes in Figure 4 revealed that "the metaphase checkpoint" might play an important role in breast cancer patients.

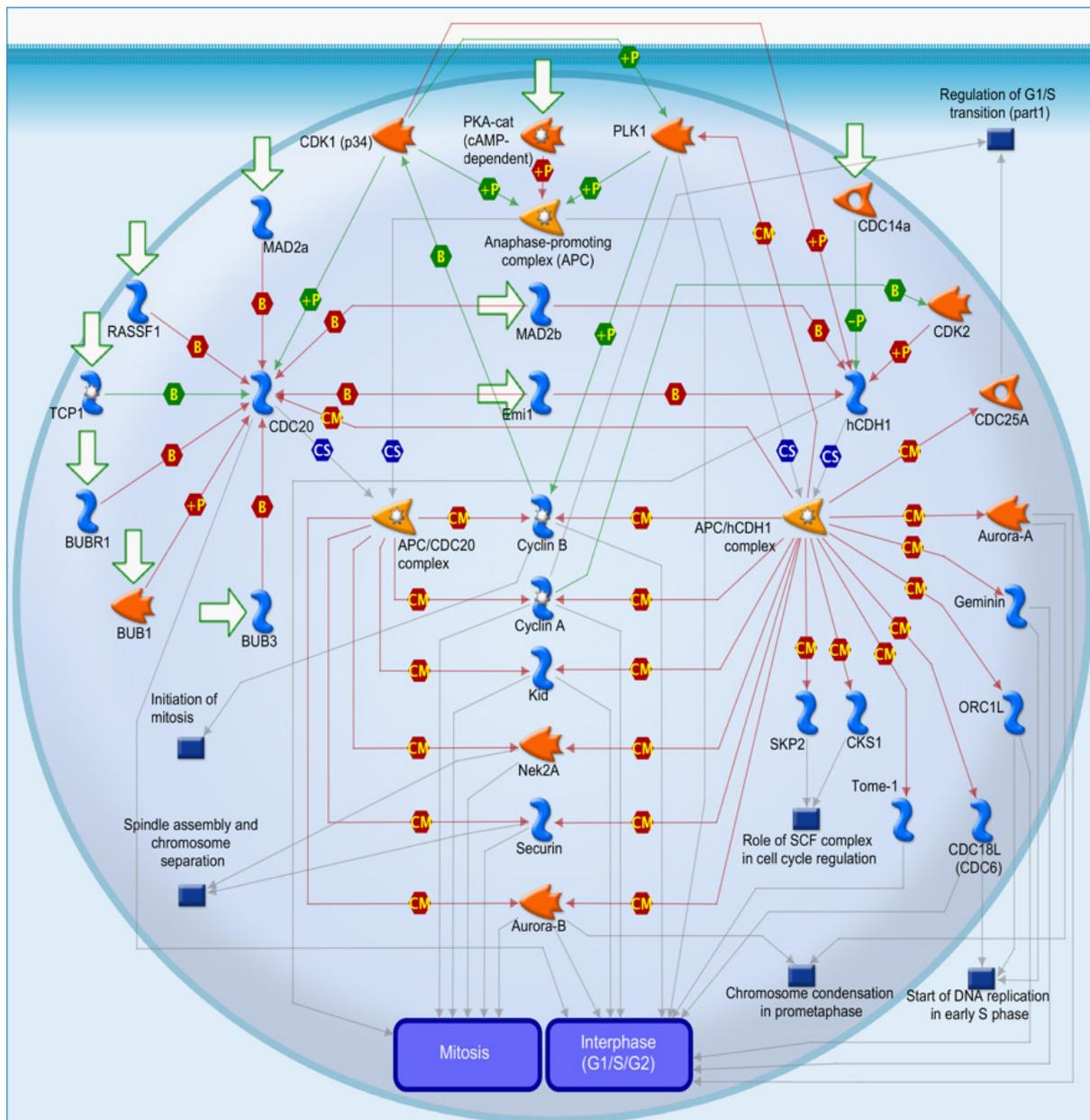


Figure S2. MetaCore pathway analysis of the coexpression gene network of pituitary tumor-transforming gene 2 (PTTG2) in breast cancer patients. Downstream pathway analyses based on the top quartile genes in Figure 6 revealed that "cell cycle role of APC in cell cycle regulation" might play an important role in breast cancer patients.

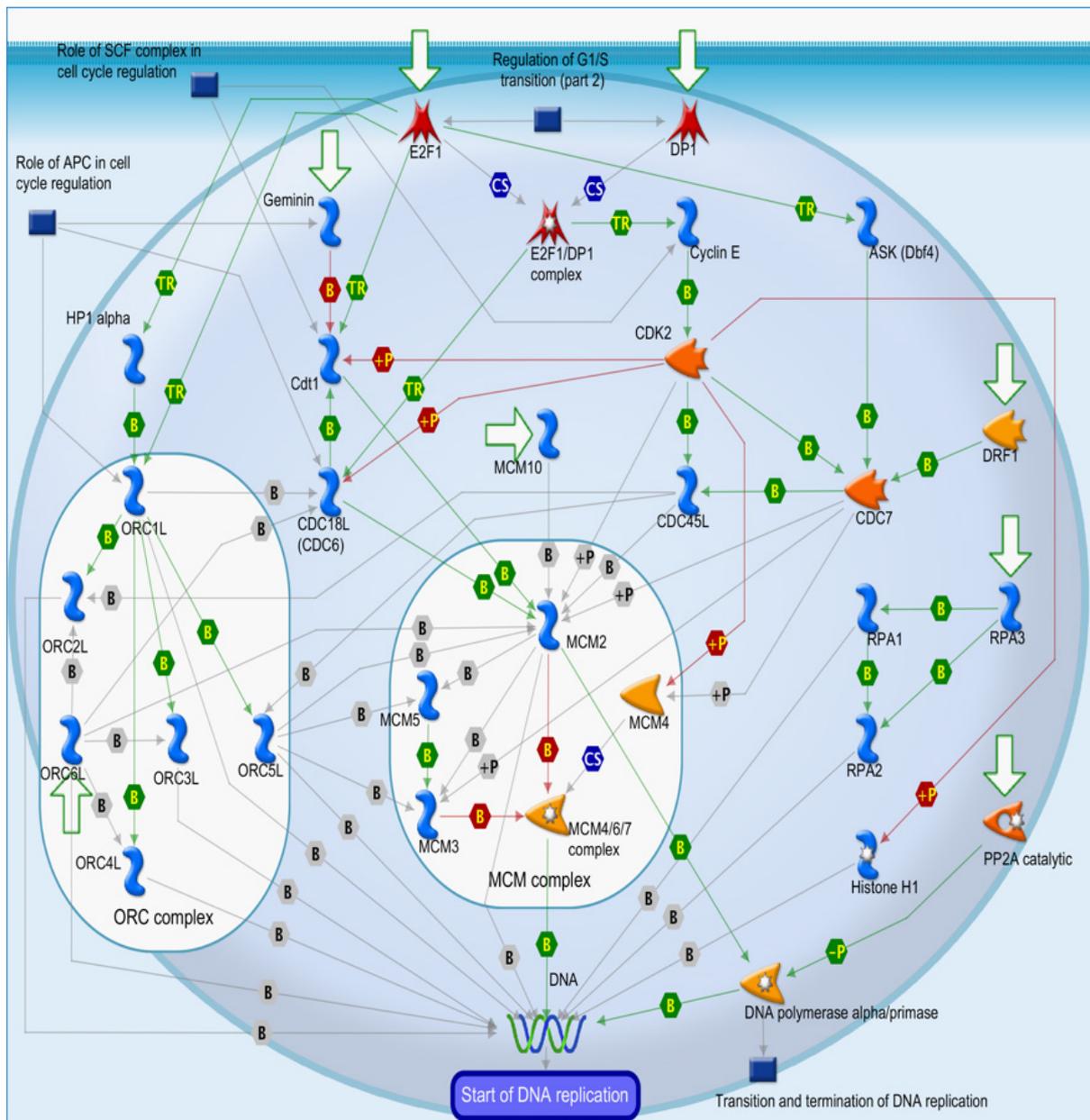


Figure S3. MetaCore pathway analysis of the coexpression gene network of pituitary tumor-transforming gene 3 (PTTG3) in breast cancer patients. Downstream pathway analyses based on the top quartile genes in Figure 8 revealed that "cell cycle and the metaphase checkpoint" might play an important role in breast cancer patients.

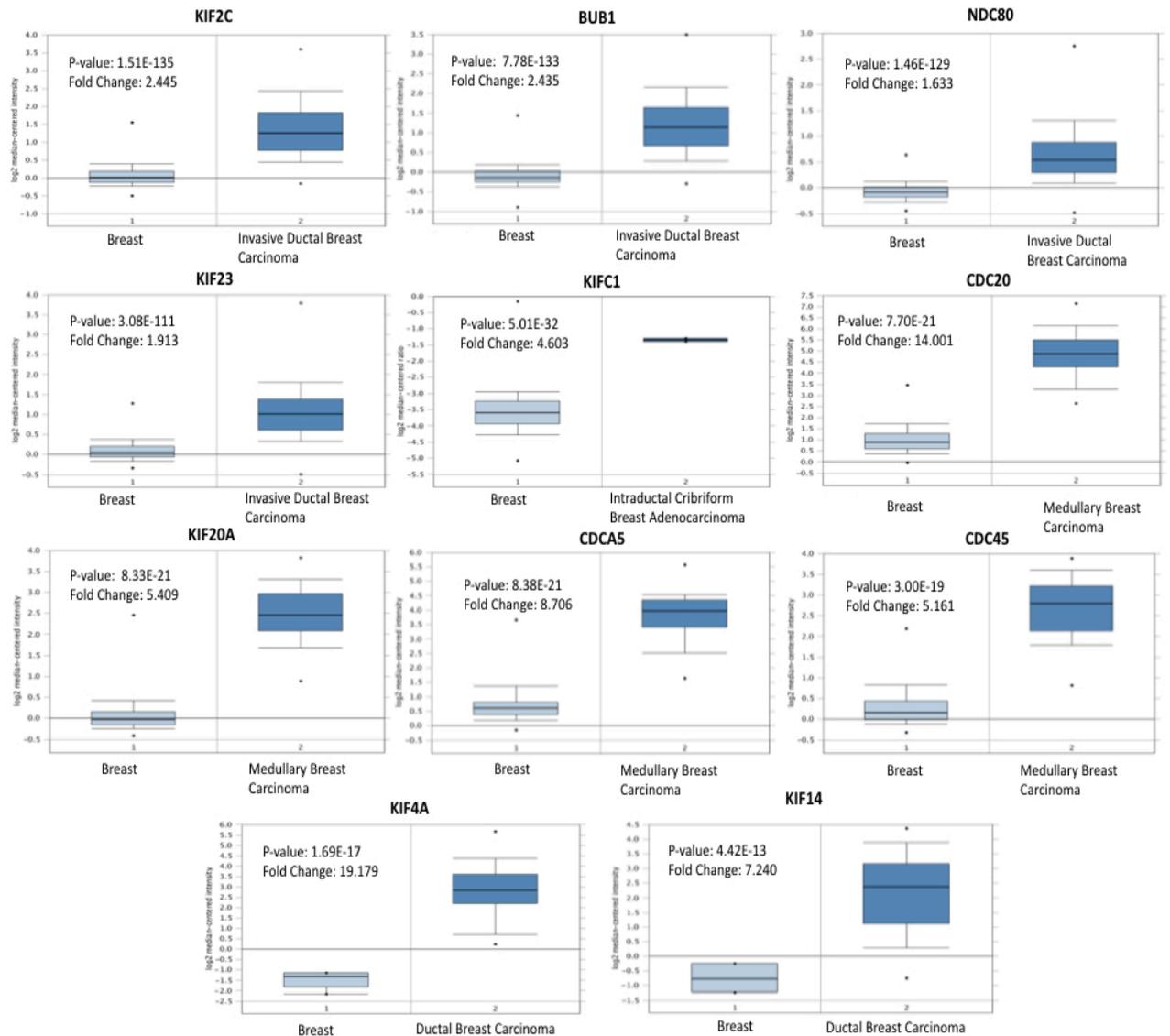


Figure S4. Meta-analysis of the PTTG family coexpressed genes in normal breast and invasive carcinoma. Further bioinformatic analysis of distinct expression patterns of genes which were found to highly correlated with PTTG family in figure 2, in normal and cancerous breast tissues.

Table S1: mRNA expression of pituitary tumor-transforming gene (PTTG) family members in different types of breast cancer patients via the OncoPrint platform

Gene	Subtype	<i>N</i> (no. of cases)	<i>p</i> value (Cancer/ Normal)	<i>t</i> -Test (Cancer/ Normal)	Fold (Cancer / Normal)	% Gene Ranking	Database References
PTTG1	Medullary Breast Carcinoma	2136	9.60E-26	2.32E+01	10.57	1 (in top 1%)	[22]
	Invasive Breast Carcinoma	2136	7.00E-11	1.09E+01	4.79	14 (in top 1%)	[22]
	Invasive Ductal and Invasive Lobular Breast Carcinoma	2136	8.38E-42	1.89E+01	4.14	33 (in top 1%)	[22]
	Invasive Lobular Breast Carcinoma	2136	1.22E-55	2.01E+01	3.67	51 (in top 1%)	[22]
	Invasive Ductal Breast Carcinoma	2136	2.20E-104	3.99E+01	4.01	109 (in top 1%)	[22]
	Mucinous Breast Carcinoma	2136	4.62E-21	1.37E+01	3.62	110 (in top 1%)	[22]
	Breast Carcinoma	2136	5.54E-07	8.12E+00	4.78	150 (in top 1%)	[22]
	Ductal Breast Carcinoma in Situ	2136	2.43E-05	6.89E+00	3.83	194 (in top 2%)	[22]
	Tubular Breast Carcinoma	2136	1.44E-25	1.39E+01	3.15	363 (in top 2%)	[22]
	Invasive Breast Carcinoma	593	5.28E-32	1.55E+01	4.42	60 (in top 1%)	[34]
	Invasive Ductal Breast Carcinoma	593	1.27E-44	2.35E+01	5.06	111 (in top 1%)	[34]
	Invasive Lobular Breast Carcinoma	593	3.01E-16	1.04E+01	2.87	155 (in top 1%)	[34]
	Mixed Lobular and Ductal Breast Carcinoma	593	6.04E-05	6.67E+00	2.73	678 (in top 4%)	[34]
	Male Breast Carcinoma	593	7.53E-05	9.95E+00	2.65	716 (in top 4%)	[34]
	Intraductal Cribriform Breast Adenocarcinoma	593	5.45E-04	1.00E+01	3.43	1003 (in top 5%)	[34]
	Lobular Breast Carcinoma	64	4.18E-06	9.50E+00	3.27	311 (in top 3%)	[82]
	Invasive Ductal Breast Carcinoma	64	4.33E-07	9.18E+00	3.49	454 (in top 4%)	[82]
	Ductal Breast Carcinoma	85	2.00E-03	5.56E+00	3.30	312 (in top 5%)	[83]
	Ductal Breast Carcinoma	167	1.00E-03	6.33E+00	3.14	340 (in top 6%)	[84]
	Ductal Breast Carcinoma	47	1.85E-07	1.15E+01	12.29	434 (in top 3%)	[85]
	Ductal Breast Carcinoma	65	1.40E-02	4.34E+00	3.59	585 (in top 9%)	[86]
	Ductal Breast Carcinoma in Situ	63	2.20E-02	2.80E+00	3.95	701 (in top 5%)	[87]
	Invasive Ductal Breast Carcinoma	63	1.60E-02	2.56E+00	3.07	924 (in top 6%)	[87]
	Invasive Mixed Breast Carcinoma	63	2.90E-02	2.29E+00	3.08	1583 (in top 10%)	[87]
	Ductal Breast Carcinoma in Situ Stroma	66	9.91E-04	3.50E+00	2.31	849 (in top 5%)	[88]
	Invasive Ductal Breast Carcinoma Epithelia	66	4.00E-03	2.93E+00	2.32	1651 (in top 9%)	[88]
	Ductal Breast Carcinoma in	66	4.00E-03	2.89E+00	2.32	1770 (in top 10%)	[88]

	Situ Epithelia							
	Invasive Breast Carcinoma	158	2.00E-03	5.67E+00	1.72	1358 (in top 8%)	[88]	
PTTG2	Invasive Ductal Breast Carcinoma	593	2.16E-37	1.94E+01	3.05	286 (in top 2%)	[34]	
	Invasive Lobular Breast Carcinoma	593	1.92E-14	9.29E+00	2.75	297 (in top 2%)	[34]	
	Invasive Breast Carcinoma	593	1.77E-23	1.21E+01	3.24	298 (in top 2%)	[34]	
	Male Breast Carcinoma	593	2.23E-06	1.10E+01	2.87	462 (in top 3%)	[34]	
	Intraductal Cribriform Breast Adenocarcinoma	593	2.17E-05	1.21E+01	2.58	540 (in top 3%)	[34]	
	Mixed Lobular and Ductal Breast Carcinoma	593	1.36E-04	6.12E+00	2.24	915 (in top 5%)	[34]	
PTTG3P	Medullary Breast Carcinoma	2136	1.52E-19	1.77E+01	6.16	17 (in top 1%)	[22]	
	Invasive Breast Carcinoma	2136	3.63E-09	9.09E+00	3.27	60 (in top 1%)	[22]	
	Invasive Ductal Carcinoma	2136	6.87E-111	3.99E+01	3.43	70 (in top 1%)	[22]	
	Invasive Lobular Breast Carcinoma	2136	7.27E-40	1.60E+01	2.37	326 (in top 2%)	[22]	
	Invasive Ductal and Invasive Lobular Breast Carcinoma	2136	3.69E-29	1.48E+01	2.79	327 (in top 2%)	[22]	
	Mucinous Breast Carcinoma	2136	1.77E-15	1.07E+01	2.46	525 (in top 3%)	[22]	
	Ductal Breast Carcinoma in Situ	2136	2.13E-04	5.29E+00	2.51	655 (in top 4%)	[22]	
	Breast Carcinoma	2136	3.76E-05	5.60E+00	2.92	826 (in top 5%)	[22]	
	Tubular Breast Carcinoma	2136	7.17E-20	1.17E+01	2.33	933 (in top 5%)	[22]	
	Male Breast Carcinoma	593	1.14E-17	1.29E+01	2.47	67 (in top 1%)	[34]	
	Invasive Ductal Breast Carcinoma	593	1.35E-45	2.41E+01	4.79	90 (in top 1%)	[34]	
	Invasive Lobular Breast Carcinoma	593	1.05E-16	1.12E+01	3.33	124 (in top 1%)	[34]	
	Invasive Breast Carcinoma	593	2.86E-27	1.37E+01	3.55	164 (in top 1%)	[34]	
	Intraductal Cribriform Breast Adenocarcinoma	593	6.92E-06	9.94E+00	3.12	461 (in top 3%)	[34]	
	Mixed Lobular and Ductal Breast Carcinoma	593	7.72E-05	6.20E+00	2.55	747 (in top 4%)	[34]	

Table S2: Pathway analysis of pituitary tumor-transforming gene 1 (PTTG1)-coexpressed genes from public breast cancer databases using the MetaCore database ($p < 0.01$ set as the cutoff value)

#	Map	<i>p</i> Value	Network objects from active data
1	Cell cycle_The metaphase checkpoint	2.3E-19	INCENP, MAD2b, SPBC25, Rod, Aurora-B, HEC, HZWint-1, Survivin, CENP-E, Nek2A, BUB1, CENP-A, HP1 alpha, Aurora-A, PLK1, CDCA1, CDC20, CENP-F, MAD2a, CENP-H, AF15q14
2	Cell cycle_Role of APC in cell cycle regulation	7.7E-18	MAD2b, CDC18L (CDC6), Tome-1, Cyclin A, Aurora-B, CDC25A, SKP2, Cyclin B, ORC1L, CKS1, Nek2A, BUB1, Geminin, Emi1, Aurora-A, PLK1, CDC20, MAD2a, CDK2
3	Cell cycle_Start of DNA replication in early S phase	2.2E-16	CDC18L (CDC6), MCM3, ORC6L, MCM4/6/7 complex, CDC7, MCM2, ORC1L, MCM5, RPA3, HP1 alpha, Geminin, DP1, MCM4, DNA polymerase alpha/primase, Cyclin E, MCM10, CDK2, CDC45L
4	Cell cycle_Chromosome condensation in prometaphase	1.7E-14	INCENP, CAP-H/H2, Condensin, CAP-C, Cyclin A, CNAP1, CAP-D2/D3, Aurora-B, Cyclin B, TOP2, Histone H3, CAP-G/G2, Aurora-A, CAP-E
5	Cell cycle_Transition and termination of DNA replication	4.4E-14	TOP2 alpha, PCNA, Cyclin A, Brca1/Bard1, Brca1, MCM2, TOP2, FEN1, POLD cat (p125), DNA ligase I, RFC complex, Bard1, DNA polymerase alpha/primase, POLD reg (p68), CDK2
6	DNA damage_ATM/ATR regulation of G1/S checkpoint	1.3E-13	PCNA, Chk2, I-kB, Cyclin A, Chk1, NFB1, CDC25A, Brca1, FANCL, CDK4, BLM, FANCD2, Bard1, Cyclin E, USP1, CDK2
7	Abnormalities in cell cycle in SCLC	3.9E-13	PCNA, Cyclin A, p14ARF, Aurora-B, SKP2, E2F2, Histone H3, CKS1, CDK4, Cyclin B1, p16INK4, Cyclin E, E2F3, Cyclin E2, CDK2
8	DNA damage_ATM / ATR regulation of G2 / M checkpoint	4.4E-12	Chk2, Cyclin A, Chk1, NFB1, Brca1, Cyclin B, Cyclin B2, FANCL, CDC25C, BLM, Cyclin B1, FANCD2, CDC25B, Kinase MYT1
9	Cell cycle_Cell cycle (generic schema)	1.9E-11	Cyclin A, CDC25A, Cyclin B, E2F2, CDC25C, CDK4, DP1, p107, Cyclin E, E2F3, CDC25B, CDK2

10	Cell cycle_Spindle assembly and chromosome separation	7.2E-11	Importin (karyopherin)-alpha, KNSL1, Aurora-B, HEC, Tubulin alpha, Cyclin B, Separase, Nek2A, TPX2, CSE1L, Aurora-A, CDC20, MAD2a, Tubulin (in microtubules)
11	DNA damage_Role of Brca1 and Brca2 in DNA repair	3.8E-09	PCNA, Histone H2AX, Chk2, NFBFD1, Brca1/Bard1, Brca1, MSH2, FANCL, FANCD2, Rad51, MSH6, Bard1
12	Cell cycle_Initiation of mitosis	8.5E-09	Lamin B, Nucleolin, KNSL1, Cyclin B2, Histone H3, CDC25C, Cyclin B1, PLK1, CDC25B, FOXM1, Kinase MYT1
13	Cell cycle_Sister chromatid cohesion	1.8E-08	PCNA, DNA polymerase sigma, Cyclin B, RFC3, Separase, Histone H3, RFC complex, CHTF18, Rad21, DCC1
14	Cell cycle_Role of SCF complex in cell cycle regulation	3.4E-08	Skp2/TrCP/FBXW, Chk1, CDC25A, SKP2, CKS1, CDK4, Emi1, Cyclin E, PLK1, NEDD8, CDK2
15	Cell cycle_Nucleocytoplasmic transport of CDK/Cyclins	5.0E-08	Importin (karyopherin)-alpha, Cyclin A, GSK3 beta, CRM1, CDK4, Cyclin B1, Cyclin E, CDK2
16	Apoptosis and survival_DNA-damage-induced apoptosis	1.0E-07	Histone H2AX, Chk2, Chk1, Brca1, FANCL, BLM, FANCD2, DNA-PK
17	dCTP/dUTP metabolism	2.2E-07	POLE1, POLA2, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, RRM2, TK1, DNA polymerase alpha/primase, POLD reg (p68), Small RR subunit, NT5C3, RRM1, DCK, Ribonucleotide reductase
18	Cell cycle_Regulation of G1/S transition (part 1)	8.0E-07	Chk2, PP2A regulatory, Cyclin A, Skp2/TrCP/FBXW, GSK3 beta, CDC25A, Brca1, CDK4, p16INK4, Cyclin E, CDK2
19	Cell cycle_Role of Nek in cell cycle regulation	1.2E-06	Tubulin beta, HEC, Tubulin alpha, Histone H3, Nek2A, Cyclin B1, TPX2, Aurora-A, MAD2a, Tubulin (in microtubules)
20	DNA damage_Mismatch repair	1.2E-06	PCNA, MutSalpha complex, DNMT1, EXO1, MSH2, Histone H3, DNA ligase I, RFC complex, MSH6, DNA-PK
21	Immune response_IFN-alpha/beta signaling via	1.4E-06	PCNA, 4E-BP1, I-kB, Cyclin A, GBP1, GSK3 beta, RSAD2, CDC25A,

	PI3K and NF-kB pathways		ISG15, CDK4, p16INK4, I-TAC, p107, Cyclin E, p19, DHFR, CDK2
22	dATP/dITP metabolism	1.4E-06	POLE1, POLA2, 8ODP, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, RRM2, DNA polymerase alpha/primase, POLD reg (p68), Small RR subunit, ADSL, RRM1, DCK, Ribonucleotide reductase, ADA
23	Reproduction_Progesterone-mediated oocyte maturation	1.4E-06	PKA-reg (cAMP-dependent), GSK3 beta, CDC25C, BUB1, Cyclin B1, Aurora-A, PLK1, H-Ras, CDC20, CDC25B, Kinase MYT1
24	Transcription_Negative regulation of HIF1A function	2.9E-06	MCM3, p14ARF, Casein kinase I delta, GSK3 beta, HIF-prolyl hydroxylase, MCM7, ARD1, MCM2, PSMA7, MCM5, PRDX4, HSP70, Elongin C, EGLN1
25	Cell cycle_ESR1 regulation of G1/S transition	2.9E-06	Cyclin A, Skp2/TrCP/FBXW, CDC25A, SKP2, CRM1, CKS1, CDK4, Cyclin A2, Cyclin E, CDK2
26	The role of aberrations in CDKN2 locus and CDK4 in familial melanoma	3.1E-06	p14ARF, E2F3/DP1 complex, E2F2, CDK4, p16INK4, DP1, p107, E2F2/DP1 complex, E2F3
27	Cell cycle_Role of 14-3-3 proteins in cell cycle regulation	3.9E-06	14-3-3 gamma, Chk2, Chk1, CDC25A, CDC25C, 14-3-3 theta, 14-3-3 zeta/delta, CDC25B
28	TTP metabolism	1.3E-05	POLE1, POLA2, Thymidylate kinase, POLA1, UDP, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, TYSY, TK1, DNA polymerase alpha/primase, POLD reg (p68)
29	Apoptosis and survival_Granzyme B signaling	1.4E-05	Tubulin alpha, MUNC13-4, NOTCH1 (NEXT), Granzyme B, tBid, Caspase-3, Lamin B1, Bid, DFF40 (CAD)
30	Epigenetic alterations in ovarian cancer	2.3E-05	DNMT3B, DNMT1, EZH2, HRK, Aurora-B, SKP2, Brca1, Histone H3, HDAC2, CDK4, p16INK4, Aurora-A, DAPK1, CDC20
31	DNA damage_DNA-damage-induced responses	2.4E-05	Chk2, Chk1, NFBFD1, Brca1, DNA-PK
32	Immune response_IL-4-induced regulators of cell growth, survival, differentiation and metabolism	2.4E-05	MCM6, Cyclin A, CDC25A, MMP-13, MCM5, CDK4, MCM4, SK4/IK1, Cyclin E, Cathepsin V, STAT1, CDK2

33	Cell cycle_Regulation of G1/S transition (part 2)	2.9E-05	Cyclin A, GSK3 beta, CDK4, Cyclin A2, DP1, p107, Cyclin E, CDK2
34	Mitogenic action of Estradiol / ESR1 (nuclear) in breast cancer	2.9E-05	CAD, CDC25A, CDK4, DNA polymerase alpha/primase, Cyclin E, SGOL2, Cyclin E2, CDK2
35	Immune response_Antigen presentation by MHC class I, classical pathway	3.2E-05	PSMB5, PSMB9, TAP1 (PSF1), PSME2, HSP70, Nardilysin, TAP, Calreticulin, PSMB2, IFN-gamma, TAP2 (PSF2)
36	Role of DNA methylation in progression of multiple myeloma	3.3E-05	DNMT1, p14ARF, NOTCH1 receptor, CDK4, SOD2, p16INK4, WNT, TDG, DAPK1, Frizzled
37	dGTP metabolism	3.4E-05	POLE1, POLA2, 8ODP, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, DNA polymerase alpha/primase, POLD reg (p68), DCK, Ribonucleotide reductase
38	Microsatellite instability in gastric cancer	4.3E-05	PCNA, MutSalphalpha complex, EXO1, MSH2, RFC complex, p16INK4, MSH6
39	Role of histone modifiers in progression of multiple myeloma	5.1E-05	EZH2, Tubulin alpha, Histone H3, HDAC2, CDK4, N-Ras, Histone H4, Caspase-3
40	Transcription_Ligand-dependent activation of the ESR1/SP pathway	5.1E-05	CAD, CDC25A, TYSY, C/EBPbeta, DNA polymerase alpha/primase, Cyclin E, Cyclin E2, ADA
41	Cell cycle progression in Prostate Cancer	6.0E-05	4E-BP1, GSK3 beta, CDC25A, Cyclin B, CDK4, WNT, Frizzled, CDC25B, CDK2
42	Transcription_Role of heterochromatin protein 1 (HP1) family in transcriptional silencing	7.4E-05	DNMT1, CDC25A, Histone H3, HDAC2, Cyclin A2, HP1 alpha, Cyclin E, HP1, Histone H4
43	Development_NOTCH1-mediated pathway for NF-KB activity modulation	1.4E-04	NOTCH1 (NICD), SAP30, NOTCH1 receptor, Histone H3, HDAC2, NOTCH1 (NEXT), Histone H4
44	Immune response_IFN-gamma actions on extracellular matrix and cell differentiation	1.7E-04	GCH1, TSA-1, Casein kinase I, EZH2, GSK3 beta, WARS, HDAC2, PSME2, IFN-gamma, STAT1
45	ATP/ITP metabolism	1.9E-04	RRP41, RPB6, RRP40, POLR2D, RRP4, PM/SCL-75, NDPK A, RRM2, HPRT, APRT, Small RR subunit, ADSL, RRM1, RPB8, Ribonucleotide

			reductase, ADA
46	Immune response_T cell co-signaling receptors, schema	2.0E-04	Nectin-2, PD-1, CTLA-4, CD80, TIGIT, CD137(TNFRSF9), PVR, ICOS, LAG3, CD70(TNFSF7)
47	Oxidative stress_Role of ASK1 under oxidative stress	2.0E-04	14-3-3 gamma, Thioredoxin, HPK38, SOD2, PRDX1, MT-TRX, DAPK1, 14-3-3 zeta/delta, Glutaredoxin, 14-3-3
48	Development_H3K36 demethylation in stem cell maintenance	2.2E-04	KDM2B, EZH2, p14ARF, Histone H3, CDK4, p16INK4
49	Dual function of Treg cells in cancer development	2.3E-04	PD-1, CTLA-4, DNMT1, ICOS, WNT, IL-2R alpha chain, Granzyme B, IFN-gamma, STAT1
50	Release of pro-inflammatory mediators and elastolytic enzymes by alveolar macrophages in COPD	2.3E-04	MMP-12, HDAC2, MMP-1, IL-8, GM-CSF, IFN-gamma, STAT1

Table S3: Pathway analysis of pituitary tumor-transforming gene 2 (PTTG2)-coexpressed genes from public breast databases using the MetaCore database ($p < 0.01$ set as the cutoff value)

#	Map	<i>p</i> Value	Network objects from active data
1	Cell cycle_Role of APC in cell cycle regulation	4.8E-16	MAD2b, Tome-1, Cyclin A, Aurora-B, CDC25A, SKP2, Cyclin B, ORC1L, CKS1, BUB1, Geminin, Emi1, Aurora-A, PLK1, CDC20, MAD2a, Securin
2	Cell cycle_The metaphase checkpoint	1.3E-13	INCENP, MAD2b, SPBC25, Aurora-B, HEC, Survivin, CENP-E, BUB1, CENP-A, HP1 alpha, Aurora-A, PLK1, CDCA1, CDC20, MAD2a, AF15q14
3	Cell cycle_Chromosome condensation in prometaphase	9.9E-11	INCENP, CAP-H/H2, CAP-C, Cyclin A, CNAP1, CAP-D2/D3, Aurora-B, Cyclin B, Histone H3, Aurora-A, CAP-E

4	Abnormalities in cell cycle in SCLC	4.4E-10	PCNA, Cyclin A, p14ARF, Aurora-B, SKP2, E2F2, Histone H3, CKS1, CDK4, p16INK4, Cyclin E, E2F3
5	Cell cycle_Cell cycle (generic schema)	2.4E-09	Cyclin A, CDC25A, Cyclin B, E2F2, CDK4, DP1, p107, Cyclin E, E2F3, CDC25B
6	Cell cycle_Spindle assembly and chromosome separation	2.6E-09	Importin (karyopherin)-alpha, Aurora-B, HEC, Tubulin alpha, Cyclin B, Separase, TPX2, Aurora-A, CDC20, MAD2a, Securin, Tubulin (in microtubules)
7	DNA damage_ATM/ATR regulation of G1/S checkpoint	2.4E-08	PCNA, Chk2, Cyclin A, Chk1, NFB1, CDC25A, CDK4, BLM, Cyclin E, Claspin, USP1
8	Cell cycle_Start of DNA replication in early S phase	2.4E-08	ORC6L, ASK (Dbf4), CDC7, ORC1L, MCM5, HP1 alpha, Geminin, DP1, Cyclin E, MCM10, CDC45L
9	Cell cycle_Sister chromatid cohesion	8.1E-08	PCNA, DNA polymerase sigma, Cyclin B, RFC3, Separase, Histone H3, Stromalins 1/2, DCC1, Securin
10	Cell cycle_Role of SCF complex in cell cycle regulation	1.0E-07	Skp2/TrCP/FBXW, Chk1, CDC25A, SKP2, CKS1, CDK4, Emi1, Cyclin E, PLK1, NEDD8
11	DNA damage_ATM / ATR regulation of G2 / M checkpoint	9.0E-07	Chk2, Cyclin A, Chk1, NFB1, Cyclin B, Cyclin B2, BLM, Claspin, CDC25B
12	The role of aberrations in CDKN2 locus and CDK4 in familial melanoma	9.0E-07	p14ARF, E2F3/DP1 complex, E2F2, CDK4, p16INK4, DP1, p107, E2F2/DP1 complex, E2F3
13	Apoptosis and survival_Granzyme B signaling	4.2E-06	Caspase-2, Tubulin alpha, NOTCH1 (NEXT), Granzyme B, tBid, Caspase-3, Lamin B1, Bid, DFF40 (CAD)
14	Cell cycle_Role of Nek in cell cycle regulation	2.9E-05	Tubulin beta, HEC, Tubulin alpha, Histone H3, TPX2, Aurora-A, MAD2a, Tubulin (in microtubules)
15	Immune response_IL-4-induced regulators of cell growth, survival, differentiation and metabolism	3.2E-05	MCM6, PERC, Cyclin A, CDC25A, MMP-13, MCM5, CDK4, SK4/IK1, Cyclin E, Cathepsin V, STAT1

16	Cell cycle_Initiation of mitosis	5.6E-05	Lamin B, Nucleolin, Cyclin B2, Histone H3, PLK1, CDC25B, FOXM1
17	Cell cycle_ESR1 regulation of G1/S transition	5.9E-05	Cyclin A, Skp2/TrCP/FBXW, CDC25A, SKP2, CKS1, CDK4, Cyclin A2, Cyclin E
18	Role of DNA methylation in progression of multiple myeloma	6.3E-05	DNMT1, p14ARF, NOTCH1 receptor, CDK4, SOD2, p16INK4, WNT, DAPK1, Frizzled
19	Dual function of Treg cells in cancer development	7.6E-05	PD-1, CTLA-4, DNMT1, ICOS, WNT, IL-2R alpha chain, Granzyme B, IFN-gamma, STAT1
20	Immune response_IFN-alpha/beta signaling via PI3K and NF-kB pathways	9.6E-05	PCNA, 4E-BP1, Cyclin A, GBP1, CDC25A, CDK4, p16INK4, I-TAC, p107, Cyclin E, p19, DHFR, eIF4A
21	Glycolysis and gluconeogenesis	9.6E-05	G3P2, TPI1, GLUT1, ENO1, PGAM1, LDHB, HXK3, ALDOC, PFKP, MDH1, PGK1, PGAM4, GPI
22	Development_H3K36 demethylation in stem cell maintenance	9.9E-05	KDM2B, EZH2, p14ARF, Histone H3, CDK4, p16INK4
23	Epigenetic alterations in ovarian cancer	1.0E-04	DNMT1, EZH2, HRK, Aurora-B, SKP2, Histone H3, HDAC2, CDK4, p16INK4, Aurora-A, DAPK1, CDC20
24	Role of histone modifiers in progression of multiple myeloma	1.5E-04	EZH2, Tubulin alpha, Histone H3, HDAC2, CDK4, N-Ras, Caspase-3
25	Transcription_Role of heterochromatin protein 1 (HP1) family in transcriptional silencing	1.6E-04	DNMT1, CDC25A, Histone H3, HDAC2, Cyclin A2, HP1 alpha, Cyclin E, HP1
26	Cell cycle_Role of 14-3-3 proteins in cell cycle regulation	1.8E-04	14-3-3 gamma, Chk2, Chk1, CDC25A, 14-3-3 theta, CDC25B
27	DNA damage_DNA-damage-induced responses	2.8E-04	Chk2, Chk1, NFBBD1, DNA-PK
28	Immune response_T cell co-signaling receptors, schema	3.2E-04	Nectin-2, PD-1, CTLA-4, TIGIT, PVR, ICOS, CD30(TNFRSF8), LAG3, PD-L1

29	Development_Epigenetic and transcriptional regulation of oligodendrocyte precursor cell differentiation and myelination	3.4E-04	NOTCH1 (NICD), SOX11, UGT8, NOTCH1 receptor, PPAR-beta(delta), HDAC2, Frizzled
30	Development_NOTCH1-mediated pathway for NF-KB activity modulation	4.8E-04	NOTCH1 (NICD), SAP30, NOTCH1 receptor, Histone H3, HDAC2, NOTCH1 (NEXT)
31	Immune response_Induction of apoptosis and inhibition of proliferation mediated by IFN-gamma	5.2E-04	IDO1, GBP1, WARS, CDK4, Cyclin E, Caspase-3, IFN-gamma, STAT1
32	Rb proteins signaling in multiple myeloma	5.8E-04	p18, CDK4, p16INK4, p107, Cyclin E
33	Cell cycle_Regulation of G1/S transition (part 1)	7.0E-04	Chk2, Cyclin A, Skp2/TrCP/FBXW, CDC25A, CDK4, p16INK4, Cyclin E
34	Neutrophil chemotaxis in asthma	7.0E-04	GRO-2, FPRL1, G-protein beta/gamma, GRO-1, HSP70, Tissue kallikreins, CCL7
35	Cell cycle_Regulation of G1/S transition (part 2)	7.3E-04	Cyclin A, CDK4, Cyclin A2, DP1, p107, Cyclin E
36	Release of pro-inflammatory mediators and elastolytic enzymes by alveolar macrophages in COPD	7.3E-04	MMP-12, HDAC2, MMP-1, GM-CSF, IFN-gamma, STAT1
37	Cell cycle progression in Prostate Cancer	8.3E-04	4E-BP1, CDC25A, Cyclin B, CDK4, WNT, Frizzled, CDC25B
38	Inter-cellular relations in COPD (general schema)	1.1E-03	GRO-1, HDAC2, I-TAC, Granzyme B, GM-CSF, IFN-gamma
39	Transcription_Ligand-dependent activation of the ESR1/SP pathway	1.1E-03	CAD, CDC25A, TYSY, C/EBPbeta, Cyclin E, ADA
40	DNA damage_Role of Brca1 and Brca2 in DNA repair	1.1E-03	PCNA, Chk2, NFBBD1, Brca2, Rad51, MSH6
41	Role of Bregs in attenuation of T and NK cells mediated anti-tumor immune responses	1.1E-03	PD-1, CTLA-4, IL-2R alpha chain, Granzyme B, LAG3, IFN-gamma, PD-L1
42	Putative pathways of MHC class I-dependent	1.2E-03	TAP1 (PSF1), PIRB, TAP, IFN-gamma, TAP2 (PSF2)

	postsynaptic long-term depression in major depressive disorder		
43	Inhibition of tumor suppressive pathways in pancreatic cancer	1.2E-03	p14ARF, Brca2, CDK4, p16INK4, Rad51
44	Basophil migration in asthma	1.5E-03	FPRL1, G-protein beta/gamma, CCL13, CCL18, FPRL2, CCL8, GM-CSF, CCL7
45	Oxidative stress_Role of ASK1 under oxidative stress	1.5E-03	14-3-3 gamma, Thioredoxin, HPK38, SOD2, MT-TRX, DAPK1, Glutaredoxin, 14-3-3
46	Immune response_Antimicrobial actions of IFN-gamma	1.5E-03	Esrra, PERC, IDO1, GBP1, C/EBPbeta, IFN-gamma, STAT1
47	Development_Notch Signaling Pathway	1.5E-03	NOTCH1 (NICD), SAP30, NOTCH1 receptor, Histone H3, HDAC2, NOTCH1 (NEXT), NOTCH1 precursor
48	DNA damage_Mismatch repair	1.5E-03	PCNA, DNMT1, EXO1, Histone H3, MSH6, DNA-PK
49	Apoptosis and survival_Regulation of Apoptosis by Mitochondrial Proteins	1.8E-03	BFL1, HRK, Bak, ANT, tBid, Bid
50	Cell cycle_Nucleocytoplasmic transport of CDK/Cyclins	1.9E-03	Importin (karyopherin)-alpha, Cyclin A, CDK4, Cyclin E

Table S4: Pathway analysis of pituitary tumor-transforming gene 3 (PTTG3P)-coexpressed genes from public breast databases using the MetaCore database (p<0.01 set as the cutoff value)

#	Map	p Value	Network objects from active data
1	Cell cycle_The metaphase checkpoint	4.59E-20	INCENP, MAD2b, SPBC25, Rod, Aurora-B, HEC, HZwint-1, Survivin, CENP-E, Nek2A, BUB1, CENP-A, HP1 alpha, Aurora-A, PLK1,

			CDCA1, CDC20, CENP-F, MAD2a, CENP-H, AF15q14
2	Cell cycle_Role of APC in cell cycle regulation	5.05E-20	MAD2b, CDC18L (CDC6), Tome-1, Cyclin A, Aurora-B, CDC25A, SKP2, Cyclin B, ORC1L, CKS1, Nek2A, BUB1, Geminin, Emi1, Aurora-A, PLK1, CDC20, MAD2a, Securin, CDK2
3	Cell cycle_Start of DNA replication in early S phase	1.54E-15	CDC18L (CDC6), MCM3, ORC6L, MCM4/6/7 complex, CDC7, MCM2, ORC1L, MCM5, HP1 alpha, Geminin, DP1, MCM4, DNA polymerase alpha/primase, Cyclin E, MCM10, CDK2, CDC45L
4	Cell cycle_Chromosome condensation in prometaphase	2.35E-13	INCENP, CAP-H/H2, Condensin, CAP-C, Cyclin A, CNAP1, CAP-D2/D3, Aurora-B, Cyclin B, TOP2, CAP-G/G2, Aurora-A, CAP-E
5	Cell cycle_Transition and termination of DNA replication	4E-13	TOP2 alpha, PCNA, Cyclin A, Brca1/Bard1, Brca1, MCM2, TOP2, FEN1, POLD cat (p125), DNA ligase I, RFC complex, Bard1, DNA polymerase alpha/primase, CDK2
6	DNA damage_ATM/ATR regulation of G1/S checkpoint	8.06E-13	PCNA, Chk2, Cyclin A, Chk1, NFBFD1, CDC25A, Brca1, FANCL, CDK4, BLM, FANCD2, Bard1, Cyclin E, USP1, CDK2
7	Cell cycle_Spindle assembly and chromosome separation	1.42E-12	Importin (karyopherin)-alpha, KNSL1, Aurora-B, HEC, Tubulin alpha, Cyclin B, Separase, Nek2A, TPX2, CSE1L, Aurora-A, CDC20, MAD2a, Securin, Tubulin (in microtubules)
8	DNA damage_ATM / ATR regulation of G2 / M checkpoint	1.53E-12	Chk2, Cyclin A, Chk1, NFBFD1, Brca1, Cyclin B, Cyclin B2, FANCL, CDC25C, BLM, Cyclin B1, FANCD2, CDC25B, Kinase MYT1
9	Abnormalities in cell cycle in SCLC	2.85E-12	PCNA, Cyclin A, p14ARF, Aurora-B, SKP2, E2F2, CKS1, CDK4, Cyclin B1, p16INK4, Cyclin E, E2F3, Cyclin E2, CDK2
10	Cell cycle_Cell cycle (generic schema)	7.72E-12	Cyclin A, CDC25A, Cyclin B, E2F2, CDC25C, CDK4, DP1, p107, Cyclin E, E2F3, CDC25B, CDK2
11	DNA damage_Role of Brca1 and Brca2 in DNA repair	1.59E-09	PCNA, Histone H2AX, Chk2, NFBFD1, Brca1/Bard1, Brca1, MSH2, FANCL, FANCD2, Rad51, MSH6, Bard1

12	Cell cycle_Sister chromatid cohesion	8.44E-09	PCNA, DNA polymerase sigma, Cyclin B, RFC3, Separase, RFC complex, CHTF18, Rad21, DCC1, Securin
13	Cell cycle_Role of SCF complex in cell cycle regulation	1.51E-08	Skp2/TrCP/FBXW, Chk1, CDC25A, SKP2, CKS1, CDK4, Emi1, Cyclin E, PLK1, NEDD8, CDK2
14	Apoptosis and survival_DNA-damage-induced apoptosis	5.67E-08	Histone H2AX, Chk2, Chk1, Brca1, FANCL, BLM, FANCD2, DNA-PK
15	Cell cycle_Initiation of mitosis	5.92E-08	Lamin B, Nucleolin, KNSL1, Cyclin B2, CDC25C, Cyclin B1, PLK1, CDC25B, FOXM1, Kinase MYT1
16	dCTP/dUTP metabolism	4.83E-07	POLE1, POLA2, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, RRM2, TK1, DNA polymerase alpha/primase, Small RR subunit, NT5C3, RRM1, DCK, Ribonucleotide reductase
17	Cell cycle_Nucleocytoplasmic transport of CDK/Cyclins	7.12E-07	Importin (karyopherin)-alpha, Cyclin A, CRM1, CDK4, Cyclin B1, Cyclin E, CDK2
18	Cell cycle_ESR1 regulation of G1/S transition	1.44E-06	Cyclin A, Skp2/TrCP/FBXW, CDC25A, SKP2, CRM1, CKS1, CDK4, Cyclin A2, Cyclin E, CDK2
19	The role of aberrations in CDKN2 locus and CDK4 in familial melanoma	1.62E-06	p14ARF, E2F3/DP1 complex, E2F2, CDK4, p16INK4, DP1, p107, E2F2/DP1 complex, E2F3
20	Cell cycle_Role of 14-3-3 proteins in cell cycle regulation	2.15E-06	14-3-3 gamma, Chk2, Chk1, CDC25A, CDC25C, 14-3-3 theta, 14-3-3 zeta/delta, CDC25B
21	dATP/dITP metabolism	2.37E-06	POLE1, POLA2, 8ODP, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, RRM2, DNA polymerase alpha/primase, Small RR subunit, ADSL, RRM1, DCK, Ribonucleotide reductase, ADA
22	Cell cycle_Regulation of G1/S transition (part 1)	3.3E-06	Chk2, PP2A regulatory, Cyclin A, Skp2/TrCP/FBXW, CDC25A, Brca1, CDK4, p16INK4, Cyclin E, CDK2
23	Transcription_Role of heterochromatin protein 1	5.47E-06	Mi-2, DNMT1, CDC25A, HDAC2, Cyclin A2, HP1 alpha, Cyclin E, HP1,

	(HP1) family in transcriptional silencing		Histone H4, Mi-2 alpha
24	Cell cycle_Role of Nek in cell cycle regulation	5.64E-06	Tubulin beta, HEC, Tubulin alpha, Nek2A, Cyclin B1, TPX2, Aurora-A, MAD2a, Tubulin (in microtubules)
25	DNA damage_Mismatch repair	5.64E-06	PCNA, MutSalpha complex, DNMT1, EXO1, MSH2, DNA ligase I, RFC complex, MSH6, DNA-PK
26	Apoptosis and survival_Granzyme B signaling	7.46E-06	Tubulin alpha, MUNC13-4, NOTCH1 (NEXT), Granzyme B, tBid, Caspase-3, Lamin B1, Bid, DFF40 (CAD)
27	Immune response_IFN-alpha/beta signaling via PI3K and NF-kB pathways	1.11E-05	PCNA, 4E-BP1, Cyclin A, GBP1, RSAD2, CDC25A, ISG15, CDK4, p16INK4, I-TAC, p107, Cyclin E, p19, DHFR, CDK2
28	Immune response_IL-4-induced regulators of cell growth, survival, differentiation and metabolism	1.12E-05	MCM6, Cyclin A, CDC25A, MMP-13, MCM5, CDK4, MCM4, SK4/IK1, Cyclin E, Cathepsin V, STAT1, CDK2
29	Immune response_Antigen presentation by MHC class I, classical pathway	1.56E-05	PSMB5, PSMB9, TAP1 (PSF1), PSME2, HSP70, Nardilysin, TAP, Calreticulin, PSMB2, IFN-gamma, TAP2 (PSF2)
30	DNA damage_DNA-damage-induced responses	1.61E-05	Chk2, Chk1, NFBFD1, Brca1, DNA-PK
31	Mitogenic action of Estradiol / ESR1 (nuclear) in breast cancer	1.66E-05	CAD, CDC25A, CDK4, DNA polymerase alpha/primase, Cyclin E, SGOL2, Cyclin E2, CDK2
32	Microsatellite instability in gastric cancer	2.61E-05	PCNA, MutSalpha complex, EXO1, MSH2, RFC complex, p16INK4, MSH6
33	Transcription_Ligand-dependent activation of the ESR1/SP pathway	2.9E-05	CAD, CDC25A, TYSY, C/EBPbeta, DNA polymerase alpha/primase, Cyclin E, Cyclin E2, ADA
34	TTP metabolism	2.98E-05	POLE1, POLA2, Thymidylate kinase, POLA1, UDP, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, TYSY, TK1, DNA polymerase alpha/primase
35	Regulation of degradation of deltaF508-CFTR in CF	3.25E-05	SEC61 complex, UFD1, Hdj-2, Csp, Sti1, HSP70, SAE1, Derlin1, UCHL1

36	Reproduction_Progesterone-mediated oocyte maturation	4.04E-05	CDC25C, BUB1, Cyclin B1, Aurora-A, PLK1, H-Ras, CDC20, CDC25B, Kinase MYT1
37	Epigenetic alterations in ovarian cancer	4.56E-05	DNMT3B, DNMT1, EZH2, HRK, Aurora-B, SKP2, Brca1, HDAC2, CDK4, p16INK4, Aurora-A, DAPK1, CDC20
38	ATP/ITP metabolism	7.69E-05	RRP41, RPB6, POLR2D, RRP4, PM/SCL-75, NDPK A, RRM2, RRP46, HPRT, APRT, Small RR subunit, ADSL, RRM1, RPB8, Ribonucleotide reductase, ADA
39	dGTP metabolism	8.19E-05	POLE1, POLA2, 8ODP, POLA1, DNA polymerase theta, POLE2, POLD cat (p125), NDPK A, DNA polymerase alpha/primase, DCK, Ribonucleotide reductase
40	Oxidative stress_Role of ASK1 under oxidative stress	1.05E-04	14-3-3 gamma, Thioredoxin, HPK38, SOD2, PRDX1, MT-TRX, DAPK1, 14-3-3 zeta/delta, Glutaredoxin, 14-3-3
41	Cell cycle_Regulation of G1/S transition (part 2)	1.45E-04	Cyclin A, CDK4, Cyclin A2, DP1, p107, Cyclin E, CDK2
42	Release of pro-inflammatory mediators and elastolytic enzymes by alveolar macrophages in COPD	1.45E-04	MMP-12, IP10, HDAC2, MMP-1, GM-CSF, IFN-gamma, STAT1
43	IL-6 signaling in colorectal cancer	1.47E-04	Ku70, DNMT1, Cyclin B, Survivin, Cyclin B1, HSP70, Cyclin E, Clusterin
44	Immune response_Induction of apoptosis and inhibition of proliferation mediated by IFN-gamma	1.54E-04	IDO1, GBP1, WARS, Brca1, CDK4, Cyclin E, Caspase-3, IFN-gamma, STAT1
45	Transcription_Negative regulation of HIF1A function	1.65E-04	MCM3, p14ARF, HIF-prolyl hydroxylase, MCM7, ARD1, MCM2, MCM5, PRDX4, HSP70, Elongin C, EGLN1
46	Role of histone modifiers in progression of multiple myeloma	2.31E-04	EZH2, Tubulin alpha, HDAC2, CDK4, N-Ras, Histone H4, Caspase-3
47	Role of Bregs in attenuation of T and NK cells	3.12E-04	PD-1, CTLA-4, CD80, IP10, IL-2R alpha chain, Granzyme B, LAG3,

	mediated anti-tumor immune responses		IFN-gamma
48	Transcription_Sin3 and NuRD in transcription regulation	3.12E-04	Mi-2, SAP30, HDAC2, PSF, p66alpha, MTA2, Histone H4, Mi-2 alpha
49	Notch signaling in breast cancer	3.97E-04	NOTCH1 (NICD), Cyclin A, HURP, NOTCH1 receptor, Survivin, Cyclin B1, NOTCH1 (NEXT), NOTCH1 precursor, CDK2
50	Immune response_IFN-gamma actions on extracellular matrix and cell differentiation	4.59E-04	GCH1, TSA-1, EZH2, WARS, IP10, HDAC2, PSME2, IFN-gamma, STAT1