

Supplementary Information for

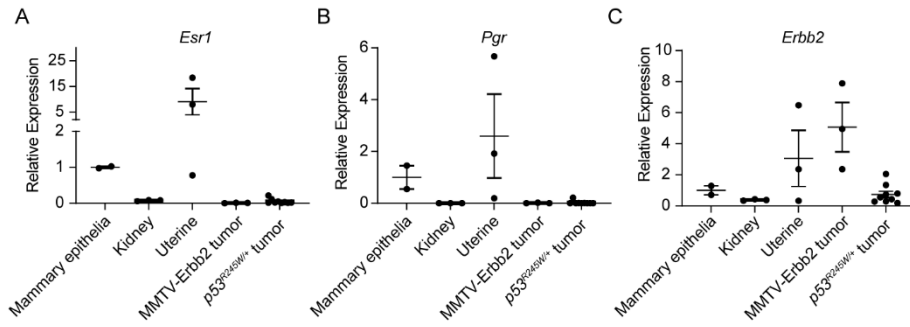
Omics analyses of a somatic *Trp53*^{R245W/+} breast cancer model identify cooperating driver events activating PI3K/AKT/mTOR signaling

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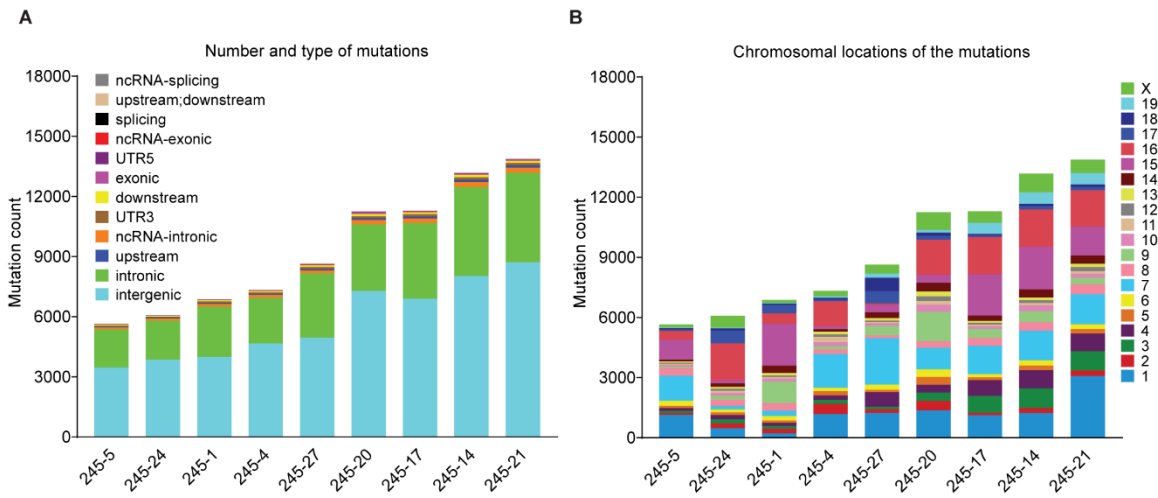
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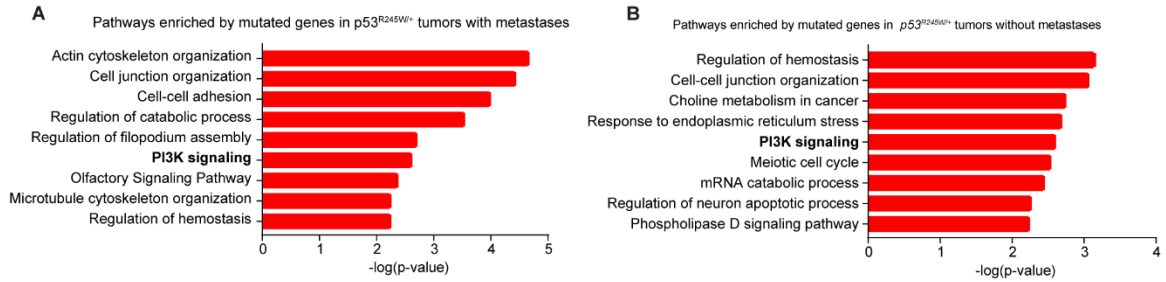
Supplementary Figures 1 to 11
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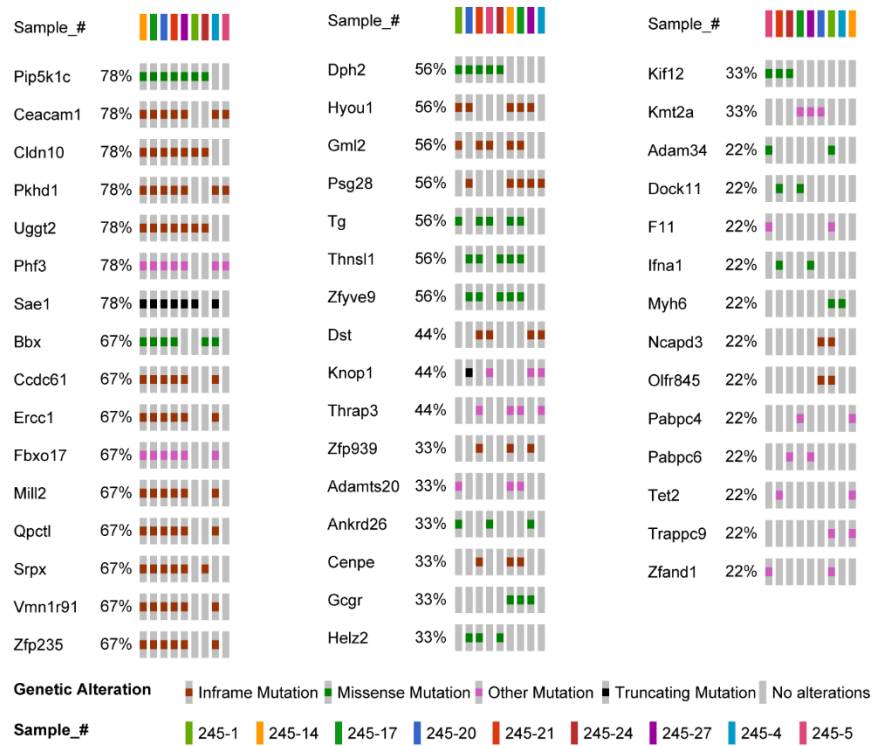
Supplementary Figure 1. The somatic *p53*^{R245W}-driven mouse mammary tumors included in the study are triple negative breast cancer. A-C. qRT-PCR analysis for *Esr1*, *Pgr* and *ErbB2*. WT mouse mammary epithelia and kidney are used as negative controls, uterine tissues are used as positive controls, mammary MMTV-ErbB2 tumors are used as positive controls for *ErbB2*, and *p53*^{R245W/+} tumors are from the nine samples included in this study.



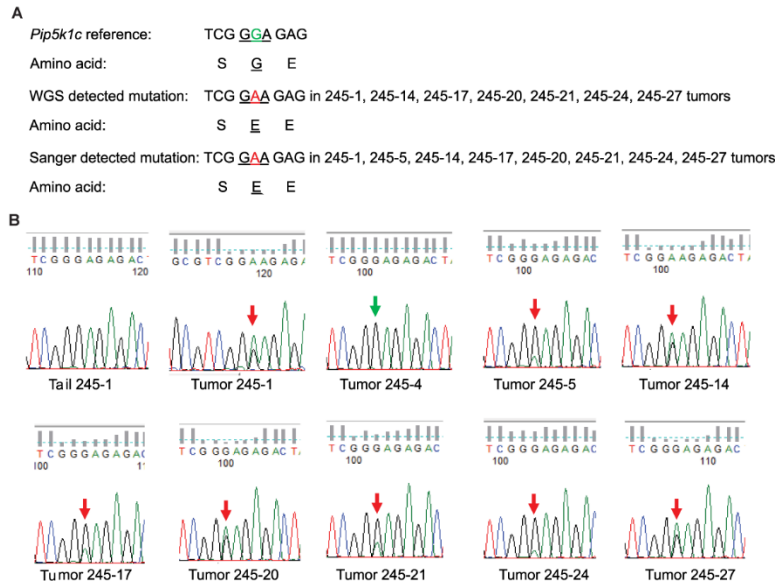
Supplementary Figure 2. Mutation landscape of somatic *p53^{R245W}*-driven mammary tumors. **A. The graph presenting total mutation count in 9 *Trp53^{R245W/+}* breast tumors. The distribution of mutations in different genetic regions was also shown. **B.** The graph depicting distribution of mutations on different chromosomes for each tumor.**



Supplementary Figure 3. WGS identifies the disruption of Pi3k/Akt/mTOR signaling in $Trp53^{R245W/+}$ breast tumors. A. GO enrichment analysis of the mutated genes identified in $Trp53^{R245W/+}$ tumors with metastasis. **B.** GO enrichment analysis of the mutated genes identified in $Trp53^{R245W/+}$ tumors without metastasis.

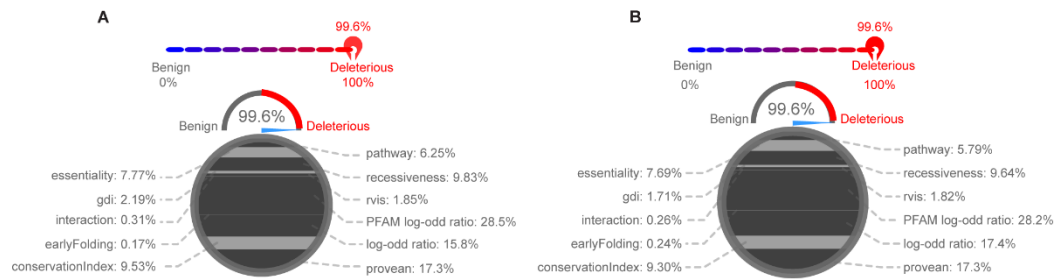


Supplementary Figure 4. Recurrent mutations identified in mouse breast tumors driven by a somatic *Trp53*^{R245W}. OncoPrint representation of the 46 recurrent mutations identified in *Trp53*^{R245W/+} tumors. Samples are arranged in rows with genes labeled along columns.

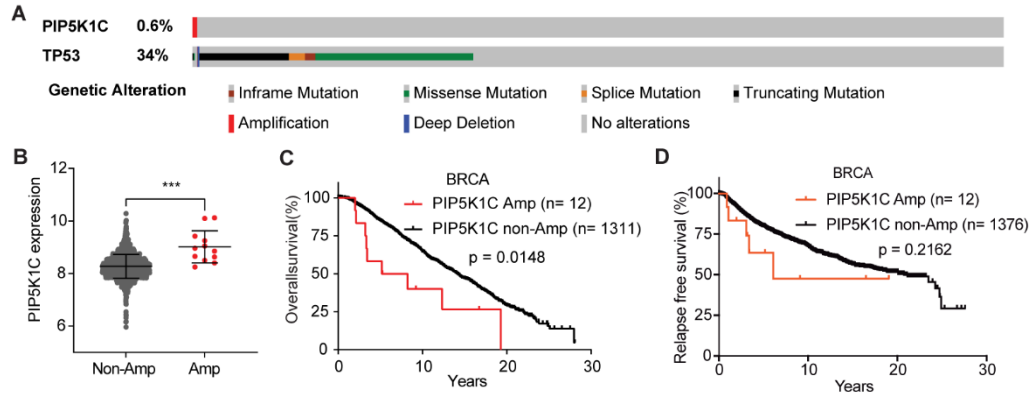


Supplementary Figure 5. Validation of *Pip5k1c*^{G67E} mutation in tumor tissues.

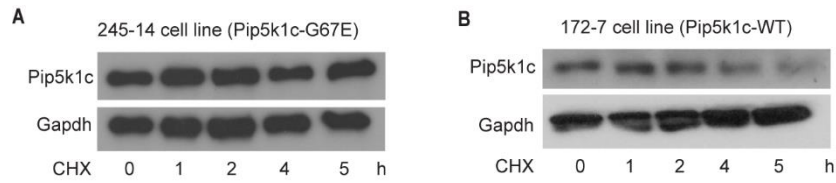
A. Illustration of the identified *Pip5k1c*^{G67E} mutation in *Trp53*^{R245W/+} tumors. Whole genome sequencing identified the *Pip5k1c*^{G67E} mutation in 7 *Trp53*^{R245W/+} tumors. Sanger sequencing confirmed the *Pip5k1c*^{G67E} mutation in the same 7 *Trp53*^{R245W/+} tumors and identified the mutation in an additional tumor sample. Green indicates wildtype; red indicates mutant. **B.** Chromatography illustration of the Sanger sequencing results in 9 *Trp53*^{R245W/+} tumors and 1 tail control. Green arrows point to wildtype *Pip5k1c*; red arrows point to *Pip5k1c*^{G67E}.



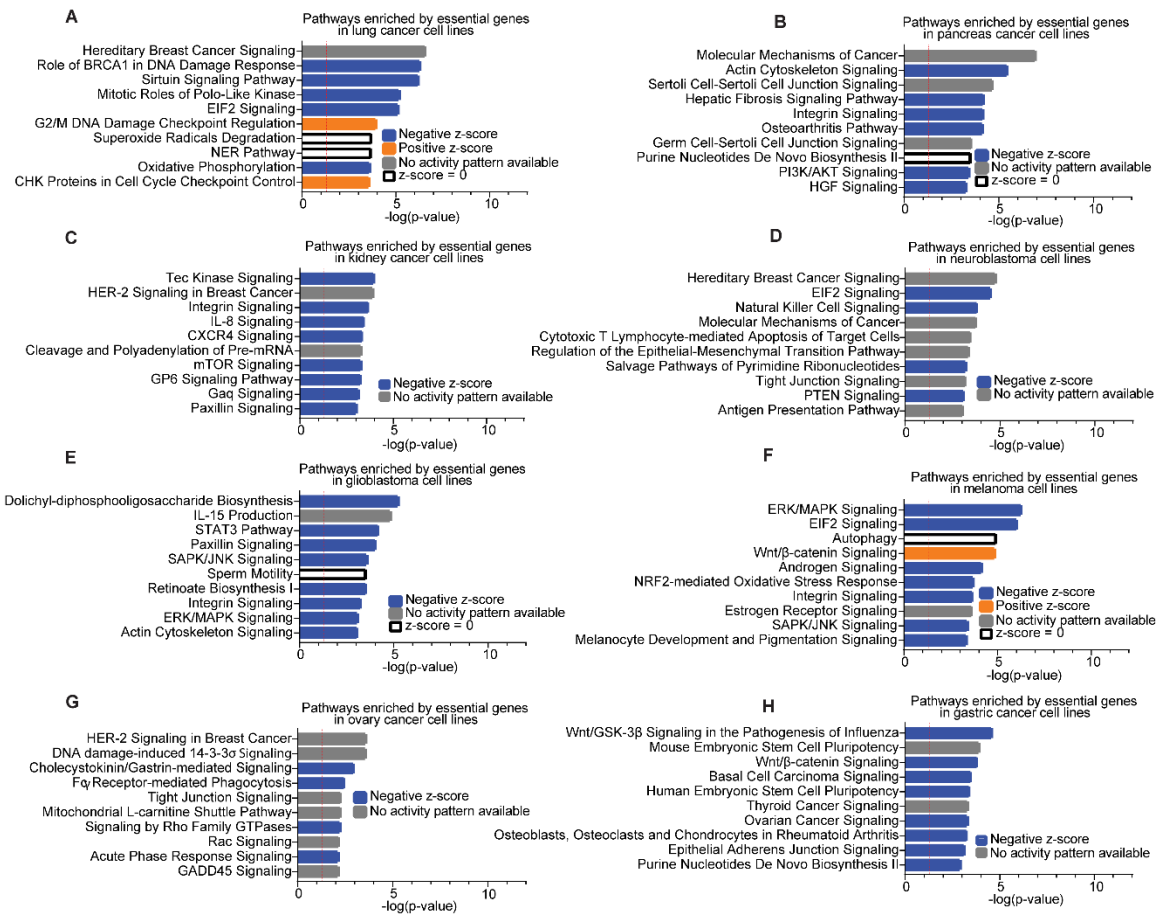
Supplementary Figure 6. p53R175H and p53R248W are predicted to be deleterious. A. Human p53R175H is predicted to be deleterious and disease-causing with a score of 0.996 by DEOGEN2. **B.** Human p53R248W is predicted to be deleterious and disease-causing with a score of 0.996 by DEOGEN2.



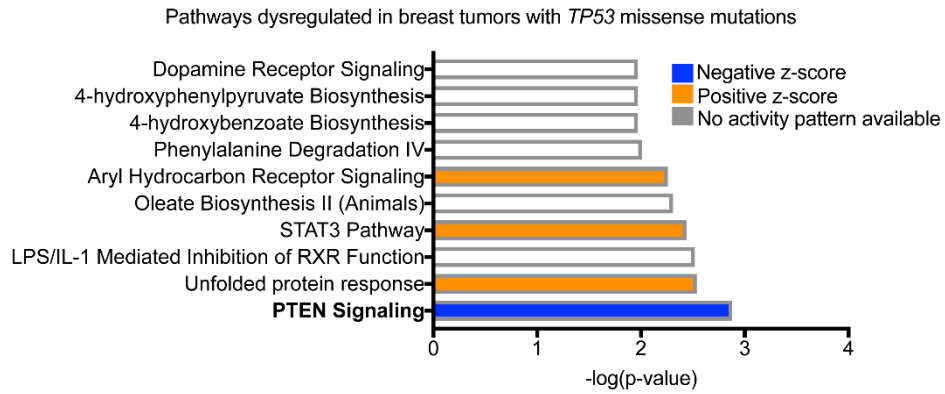
Supplementary Figure 7. *PIP5K1C* is amplified in human breast cancer and associates with worse survival. **A.** Oncoprint representation of *PIP5K1C* and *TP53* mutations in human breast tumors (n=2173). **B.** Association of *PIP5K1C* expression with copy numbers in human breast tumors. **C.** Comparison of overall survival in human breast cancer (BRCA) patients with or without *PIP5K1C* amplification. **D.** Comparison of relapse-free survival in BRCA patients with or without *PIP5K1C* amplification. ***, $p < 0.001$.



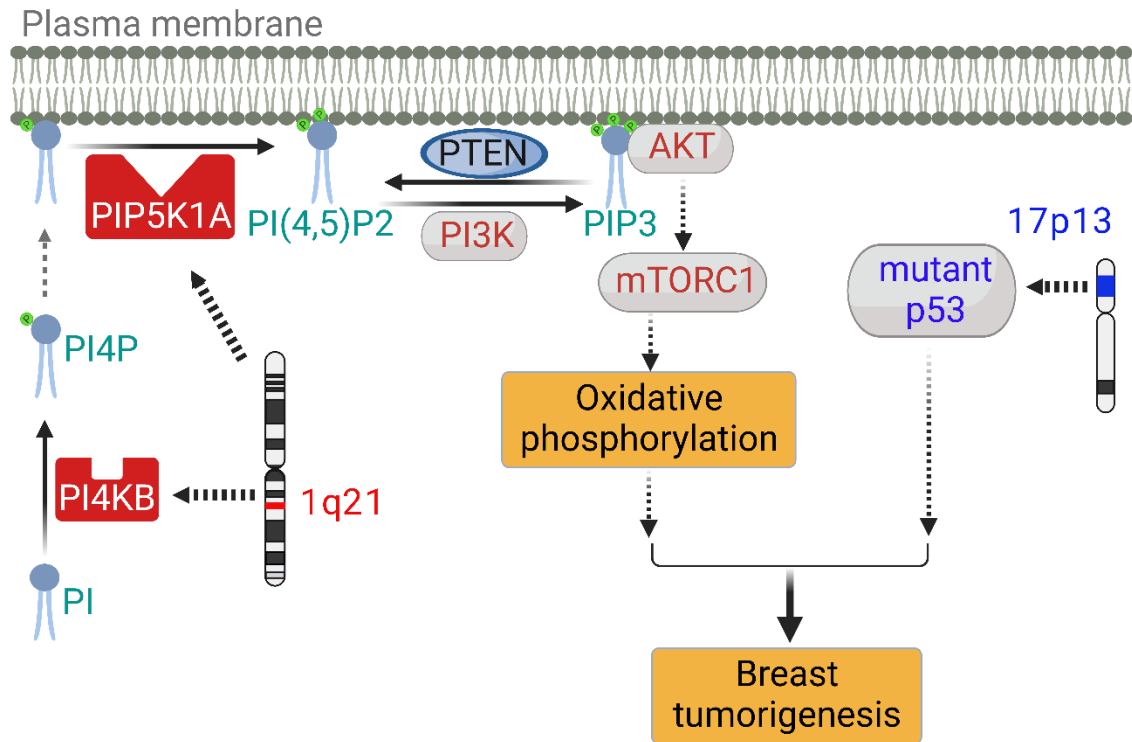
Supplementary Figure 8. *Pip5k1c*^{G67E} mutation stabilizes Pip5k1c protein. A. Western blot showing the stability of Pip5k1c protein in tumor-derived cell line 245-14 treated with 33 µg/mL cycloheximide (CHX) and harvested at different time points. **B.** Western blot showing the stability of Pip5k1c protein in tumor-derived cell line 172-7 treated with 33 µg/mL cycloheximide (CHX) and harvested at different time points.



Supplementary Figure 9. Essential pathways identified by IPA in various types of cancer cell lines. IPA analysis of the essential genes in various types of cancers generated top 10 essential pathways in each type of cancer.



Supplementary Figure 10. PTEN signaling is downregulated in human breast cancer with *TP53* missense mutations. IPA analysis of the significantly upregulated genes in *TP53* mutant breast cancer compared to *TP53* wildtype breast cancer.



Supplementary Figure 11. Proposed model. Figure shows a summary of the role of *PI4KB/PIP5K1A* amplification in activating PI3K signaling to drive breast tumorigenesis. Graph was created with BioRender.com.

Supplementary Table 1. Putative driver mutations identified by WGS in mouse breast tumors driven by somatic *Trp53*^{R245W}

Gene	Amino Acid Change	Samples with mutations	Gene function	Source
<i>Abi1</i>	p.E250Q	245-20	TSG	OncoKB
<i>Cenpe</i>	p.K1176S	245-14, 245-17, 245-21	Oncogene	Ref(35, 36)
<i>ErbB2</i>	p.S1079A	245-20	Oncogene	OncoKB
<i>Grin2a</i>	p.V203M	245-21	TSG	OncoKB
<i>Kmt2a</i>	p.G66delinsAG	245-17, 245-20, 245-27	TSG	OncoKB
<i>Kras</i>	p.G12D	245-1	Oncogene	OncoKB
<i>Nf1</i>	p.R2271X	245-5	TSG	OncoKB
<i>Pax3</i>	p.Q407P	245-21	Oncogene	OncoKB
<i>Pten</i>	p.R233fs	245-27	TSG	OncoKB
<i>Reln</i>	p.G182E	245-20	TSG	OncoKB
<i>Tet2</i>	p.L700delinsQQL	245-14, 245-21	TSG	OncoKB
<i>Tle1</i>	p.Q735H	245-24	Oncogene	OncoKB
<i>Wdr11</i>	p.F927V	245-14	TSG	Ref(40)

TSG: tumor suppressor gene

Supplementary Table 2. Summary of breast cancer cell lines used in genetic screens in DepMap.

Cell line	TP53 status	p53 Amino Acid Change	Hormone status
KPL1	WT		ER+ HER2-
MCF7	WT		ER+ HER2-
ZR751	WT		ER+ HER2-
CAL51	WT		TNBC
DU4475	WT		TNBC
SKBR3	MUT	p.R175H	ER- HER2+
JIMT1	MUT	p.R248W	ER- HER2+
HCC202	MUT	p.T284fs	ER- HER2+
HCC1954	MUT	p.Y163C	ER- HER2+
HCC1428	MUT	p.?	ER+ HER2-
CAMA1	MUT	p.R280T	ER+ HER2-
MDAMB415	MUT	p.Y236C	ER+ HER2-
SUM52PE	MUT	p.R213*	ER+ HER2+
HCC1419	MUT	p.Y220C	ER+ HER2+
AU565	MUT	p.R175H	HER2+
CAL120	MUT	p.?	TNBC
MDAMB157	MUT	p.?	TNBC
MDAMB436	MUT	p.?	TNBC
MDAMB453	MUT	p.?	TNBC
SUM159PT	MUT	p.?	TNBC
HCC1187	MUT	p.G108del	TNBC
EFM19	MUT	p.H193R	TNBC
SUM149PT	MUT	p.M237I	TNBC
HMC18	MUT	p.P152fs	TNBC
HCC1395	MUT	p.R175H	TNBC
HCC1143	MUT	p.R248Q	TNBC
BT549	MUT	p.R249S	TNBC

SUM229PE	MUT	p.R273C	TNBC
MDAMB468	MUT	p.R273H	TNBC
HCC38	MUT	p.R273L	TNBC
MDAMB231	MUT	p.R280K	TNBC
HCC1937	MUT	p.R306*	TNBC
HCC1806	MUT	p.T256fs	TNBC
HS578T	MUT	p.V157F	TNBC

WT, wildtype.
MUT, mutant.

Supplementary Table 3. Receptor status of breast cancer patients with co-amplification of *PI4KB* and *PIP5K1A* in METABRIC data.

Sample ID	Cancer Type Detailed	ER status measured by IHC	HER2 Status
MB-0115	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0206	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0303	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0446	Breast Invasive Ductal Carcinoma	Negative	Negative
	Breast Invasive Lobular		
MB-0582	Carcinoma	Negative	Negative
MB-0658	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-2827	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3057	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3058	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3297	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3396	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3476	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4622	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4732	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4769	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4938	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5126	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5173	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5258	Breast Invasive Ductal Carcinoma	Negative	Negative
	Breast Invasive Lobular		
MB-5298	Carcinoma	Negative	Negative
MB-5335	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5442	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5450	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5526	Breast Invasive Ductal Carcinoma	Negative	Negative

MB-5551	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5560	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5565	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6143	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6188	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6248	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7007	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7009	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7023	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7036	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7114	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7145	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7155	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7205	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7269	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0375	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0506	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4987	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0062	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0191	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-0200	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-3001	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4254	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4332	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4407	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-4793	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5102	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5135	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5624	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6098	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6280	Breast Invasive Ductal Carcinoma	Negative	Negative

MB-7031	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7055	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7159	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7225	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-7267	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-6273	Breast Invasive Ductal Carcinoma	Negative	Negative
MB-5468	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-6114	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-4012	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-5441	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-0201	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-0314	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-0395	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-3025	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-3329	Breast Invasive Ductal Carcinoma	Negative	Positive
	Breast Mixed Ductal and Lobular		
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MB-4663	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-4871	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-5199	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-5229	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-6337	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-7020	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-7135	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-7260	Breast Invasive Ductal Carcinoma	Negative	Positive
MB-0522	Invasive Breast Carcinoma	Negative	Positive
MB-4350	Breast Invasive Ductal Carcinoma	Negative	Positive
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MB-0500	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-4694	Breast Invasive Ductal Carcinoma	Positive	Negative

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MB-0146	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-0198	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-0261	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-0356	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-5167	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-7254	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-7288	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
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	Breast Invasive Lobular		
MB-0101	Carcinoma	Positive	Negative

MB-0122	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-0891	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-2564	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-2610	Carcinoma	Positive	Negative
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MB-2750	Carcinoma	Positive	Negative
	Breast Invasive Mixed Mucinous		
MB-2919	Carcinoma	Positive	Negative
MB-2931	Breast Invasive Ductal Carcinoma	Positive	Negative
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MB-2990	Carcinoma	Positive	Negative
MB-3032	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-3033	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-3037	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-3079	Carcinoma	Positive	Negative
MB-3298	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-3412	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-3439	Carcinoma	Positive	Negative
MB-3450	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-3781	Carcinoma	Positive	Negative
MB-3871	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4120	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4140	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4141	Breast Invasive Ductal Carcinoma	Positive	Negative

	Breast Mixed Ductal and Lobular		
MB-4293	Carcinoma	Positive	Negative
MB-4599	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4701	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4709	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4719	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4721	Carcinoma	Positive	Negative
MB-4735	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4741	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-4742	Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4764	Carcinoma	Positive	Negative
MB-4785	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4825	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4827	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4843	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4853	Carcinoma	Positive	Negative
MB-4869	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4872	Carcinoma	Positive	Negative
MB-4899	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4961	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4967	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4977	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-4981	Carcinoma	Positive	Negative
MB-5015	Breast Invasive Ductal Carcinoma	Positive	Negative

	Breast Mixed Ductal and Lobular		
MB-5020	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5027	Carcinoma	Positive	Negative
MB-5084	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5088	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5092	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5183	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5221	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5253	Carcinoma	Positive	Negative
MB-5264	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5290	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5300	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-5330	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5358	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5360	Carcinoma	Positive	Negative
MB-5364	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5369	Carcinoma	Positive	Negative
MB-5383	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5395	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5403	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5407	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5412	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5424	Carcinoma	Positive	Negative

	Breast Mixed Ductal and Lobular		
MB-5451	Carcinoma	Positive	Negative
MB-5457	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5473	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-5478	Carcinoma	Positive	Negative
MB-5490	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-5492	Carcinoma	Positive	Negative
MB-5589	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-5626	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-6006	Carcinoma	Positive	Negative
MB-6018	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6024	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6050	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6083	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6118	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-6138	Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-6167	Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-6195	Carcinoma	Positive	Negative
MB-6207	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6211	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-6229	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-6233	Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-6253	Carcinoma	Positive	Negative

MB-6256	Breast Invasive Ductal Carcinoma Breast Invasive Lobular	Positive	Negative
MB-7004	Carcinoma	Positive	Negative
MB-7005	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7006	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7013	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7026	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7037	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7106	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7167	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7185	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7220	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7228	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7277	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-7279	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-2771	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4354	Breast Invasive Ductal Carcinoma Breast Mixed Ductal and Lobular	Positive	Negative
MB-0093	Carcinoma	Positive	Negative
MB-0097	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-0256	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-0268	Breast Invasive Ductal Carcinoma Breast Mixed Ductal and Lobular	Positive	Negative
MB-0367	Carcinoma	Positive	Negative
MB-0512	Breast Invasive Ductal Carcinoma Breast Mixed Ductal and Lobular	Positive	Negative
MB-0646	Carcinoma	Positive	Negative
MB-2952	Breast Invasive Ductal Carcinoma Breast Invasive Lobular	Positive	Negative
MB-4005	Carcinoma	Positive	Negative
MB-4222	Breast Invasive Ductal Carcinoma	Positive	Negative

MB-4339	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4353	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4368	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4390	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4442	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-4557	Carcinoma	Positive	Negative
MB-4593	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4598	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4603	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4607	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4744	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-4798	Carcinoma	Positive	Negative
MB-4838	Breast Invasive Ductal Carcinoma	Positive	Negative
MB-4976	Breast Invasive Ductal Carcinoma	Positive	Negative
	Breast Invasive Lobular		
MB-6012	Carcinoma	Positive	Negative
	Breast Mixed Ductal and Lobular		
MB-0589	Carcinoma	Positive	Positive
MB-3028	Breast Invasive Ductal Carcinoma	Positive	Positive
	Breast Invasive Lobular		
MB-4289	Carcinoma	Positive	Positive
MB-2847	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-0389	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-0421	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-0465	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-0662	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-2626	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-2786	Breast Invasive Ductal Carcinoma	Positive	Positive

	Breast Invasive Lobular		
MB-3379	Carcinoma	Positive	Positive
MB-4276	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-4688	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-4796	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-5078	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-5418	Breast Invasive Ductal Carcinoma	Positive	Positive
MB-0046	Breast Invasive Ductal Carcinoma	Positive	Positive
MTS-T0139	Breast Invasive Ductal Carcinoma	Negative	
MTS-T0160	Invasive Breast Carcinoma	Negative	
MTS-T0275	Breast Invasive Ductal Carcinoma	Negative	
MTS-T0689	Breast Invasive Ductal Carcinoma	Negative	
MTS-T0694	Breast Invasive Ductal Carcinoma	Negative	
MTS-T0714	Breast Invasive Ductal Carcinoma	Negative	
MTS-T1291	Breast Invasive Ductal Carcinoma	Negative	
MTS-T2407	Breast Invasive Ductal Carcinoma	Negative	
MB-0025	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0090	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0092	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0134	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0142	Breast Invasive Ductal Carcinoma	Positive	
	Breast Mixed Ductal and Lobular		
MTS-T0153	Carcinoma	Positive	
MTS-T0154	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0602	Breast Invasive Ductal Carcinoma	Positive	
MTS-T0711	Invasive Breast Carcinoma	Positive	
MTS-T0715	Breast Invasive Ductal Carcinoma	Positive	
MTS-T1279	Invasive Breast Carcinoma	Positive	
MTS-T1283	Breast Invasive Ductal Carcinoma	Positive	
MTS-T1306	Breast Invasive Ductal Carcinoma	Positive	
MTS-T1309	Invasive Breast Carcinoma	Positive	

MTS-T1311	Breast Invasive Ductal Carcinoma Breast Mixed Ductal and Lobular	Positive	
MTS-T1991	Carcinoma	Positive	
MTS-T2190	Invasive Breast Carcinoma	Positive	
MTS-T2206	Invasive Breast Carcinoma	Positive	
MTS-T2409	Breast Invasive Ductal Carcinoma	Positive	
MTS-T2412	Breast Invasive Ductal Carcinoma	Positive	
MB-4880	Breast Invasive Ductal Carcinoma		Negative
MB-0242	Breast Invasive Ductal Carcinoma		Negative
MB-4722	Breast Invasive Ductal Carcinoma		Negative
MB-7118	Breast Invasive Ductal Carcinoma		Negative
MB-0110	Invasive Breast Carcinoma		Negative
MB-7115	Breast Invasive Ductal Carcinoma Breast Invasive Lobular		Positive
MTS-T0066	Carcinoma		
MTS-T0068	Breast Invasive Ductal Carcinoma Breast Invasive Lobular		
MTS-T0076	Carcinoma Breast Mixed Ductal and Lobular		
MTS-T0077	Carcinoma Breast Invasive Lobular		
MTS-T0085	Carcinoma Breast Invasive Lobular		
MTS-T0091	Carcinoma		
MTS-T0250	Invasive Breast Carcinoma		

Supplementary Table 4. Summary of receptor status of breast cancer patients with co-amplification of *PI4KB* and *PIP5K1A* in METABRIC data.

# of patients	ER	HER2
258	+	-
61	-	-
20	-	+
20	+	NA
17	+	+
8	-	NA
7	NA	NA
5	NA	-
1	NA	+

NA, not available.