SUPPLEMENTARY INFORMATION FOR:

Recurrent gross mutations of the PTEN tumor suppressor gene in breast cancers with deficient DSB repair

Lao H. Saal, Sofia K. Gruvberger-Saal, Camilla Persson, Kristina Lövgren, Mervi Jumppanen, Johan Staaf, Göran Jönsson, Maira M. Pires, Matthew Maurer, Karolina Holm, Susan Koujak, Shivakumar Subramaniyam, Johan Vallon-Christersson[3], Håkan Olsson, Tao Su, Lorenzo Memeo, Thomas Ludwig, Stephen P. Ethier, Morten Krogh, Matthias Szabolcs, Vundavalli V.V.S. Murty, Jorma Isola, Hanina Hibshoosh, Ramon Parsons*, and Åke Borg*

Contains Supplementary Tables 1-3 and Supplementary Figure 1.

Supplementary Table 1 Evaluation of *Pten*$^{+/-}$ heterozygous mouse mammary epithelial tumors

					Gland-forming Tumor Epithelial Cells			Metaplastic Tumor Epithelial Cells		
Tumor #	Mouse ID	Age (days)	Mammary Tumor Type[a]	Basal-like Marker Positive	Ck5/6 IHC	Ck14 IHC	ER IHC	Ck5/6 IHC	Ck14 IHC	ER IHC
1	91	364	Metaplastic carcinoma	Yes	0	1+	2+	2+	3+	0
2	92	364	Adenocarcinoma (type C)	Yes	0	0	2+	2+	2+	0
3	121	293	Squamous carcinoma	Yes	3+	3+	2+	np	np	np
4	143	308	Adenocarcinoma (type B)	Yes	3+	3+	0	np	np	np
5	161	410	Adenocarcinoma (type C)	Yes	0	0	2+	2+	2+	0
6	162	435	Adenocarcinoma (type C)	Yes	0	0	2+	2+	3+	0
7	164	264	Metaplastic carcinoma	Yes	2+	2+	1+	2+	3+	0
8	206	339	Metaplastic carcinoma	Yes	1+	1+	2+	2+	3+	0
9	206	339	Adenocarcinoma (type B)	Yes	1+	1+	0	np	np	np
10	219	142	Metaplastic carcinoma	Yes	1+	2+	1+	3+	3+	0
11	275	369	Metaplastic carcinoma	Yes	0	0	2+	3+	3+	0
12	485	342	Adenosquamous carcinoma	Yes	3+	3+	2+	np	np	np
13	556	293	Metaplastic carcinoma	Yes	1+	2+	2+	2+	3+	0

[a] Tumor categorization is based on the Dunn's classification.

Cytokeratin (CK) mmunostaining (IHC) was scored as follows: 0, no staining; 1+, moderate staining; 2+, focally strong (<15% of cells); 3+, strong in >15% of cells.
Estrogen receptor (ER) IHC was scored as follows: 0, <1% positive nuclei, 1+, 1-4% positive nuclei; 2+, ≥5% positive nuclei.
np=respective component not present in tumor.

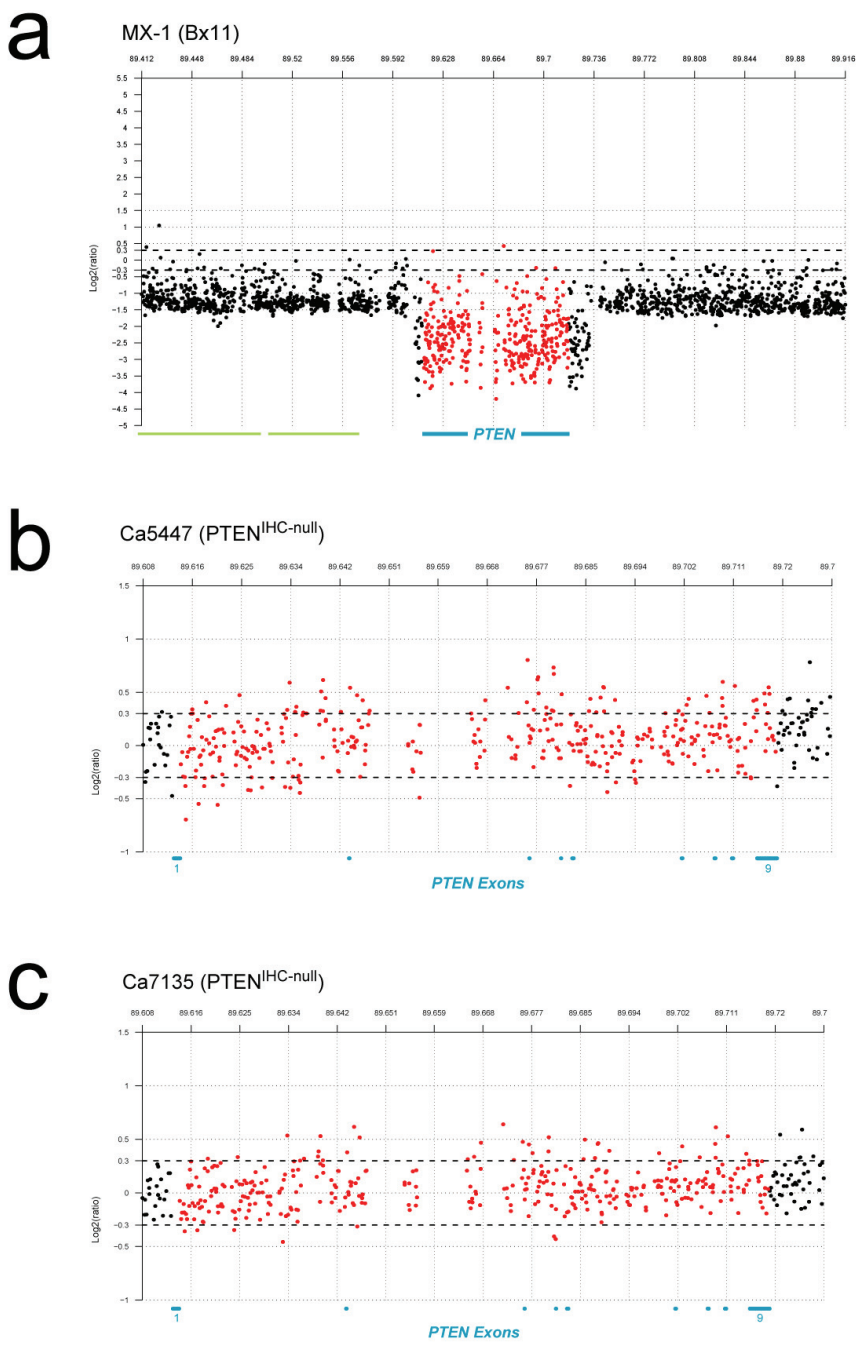
Supplementary Table 2 PTEN and basal-like phenotype in human non-hereditary breast carcinoma

	All Cases				Estrogen Receptor-Negative Subset			
	PTEN IHC-loss	PTEN IHC-positive	N	P-value	PTEN IHC-loss	PTEN IHC-positive	N	P-value
CK5/14 IHC Positive	19	16	297	4.0E-09	18	14	87	0.0122
CK5/14 IHC Negative	35	227			16	39		

Supplementary Table 3 Immunohistochemical and genetic analyses of human BRCA1 hereditary breast cancer samples

Sample	Origin	*BRCA1* Mutation	BRCA1 AA Change	*PTEN* Sequence	PTEN IHC	GPM	*PTEN* Genomic Locus	Figure
Ca2654	Primary Tumor	3171ins5	fs>1025X	WT	Loss (Null)	Yes	Macro-CNI by Agilent HD-aCGH / CN Gain by BAC aCGH	5b
Ca5447	Recurrence	1806C>T	Q563X	WT	Loss (Null)	No	Apparent Normal CN by Agilent HD-aCGH / Normal CN by BAC aCGH	SF 1b
Ca7135	Primary Tumor	1806C>T	Q563X		Loss (Null)	No	Apparent Normal CN by Agilent HD-aCGH / Normal CN by BAC aCGH	SF 1c
Ca7178	Recurrence	2594delC	fs>845X		Loss (Null)			
Ca7263	Primary Tumor	IVS17-2A>C [a]	splice acceptor		Loss (Null)			
Ca8571	Primary Tumor	1806C>T	Q563X	WT	Loss (Null)			
Ca8822	Primary Tumor	1201del11	fs>361X		Loss			
Ca10581	Primary Tumor	1806C>T	Q563X		Loss			
Ca10697	Primary Tumor	IVS21-36del510	fs>1804X	WT	Loss (Null)			
Ca11394	Primary Tumor	1177G>A	W353X	WT	Loss			
Ca12421	Primary Tumor	2594delC	fs>845X	WT	Loss		Normal CN by BAC aCGH	
Ca12532	LN Metastasis	5242C>A	A1708E		Loss (Null)	Yes	Homozygous Deletion by Agilent HD-aCGH / CN Loss (potential HD) by BAC aCGH	5a
Ca12864	Primary Tumor	3171ins5	fs>1025X		Loss (Null)	Yes	Micro-CNI by Agilent HD-aCGH / CN Loss (LOH) by BAC aCGH	3c, 5d
Ca13494	Primary Tumor	3438G>T	E1107X		Loss (Null)	Yes	Homozygous Deletion by Agilent HD-aCGH / Homozygous Deletion by BAC aCGH	5e
Ca13714	Primary Tumor	5382insC	fs>1829X		Loss (Null)	Yes	Micro-CNI by Agilent HD-aCGH / CN Loss (LOH) by BAC aCGH	5c
Ca13812	Primary Tumor	4808C>G	Y1563X		Positive		Normal CN by BAC aCGH	
Ca13996	LN Metastasis	1806C>T	Q563X	WT	Positive		CN Loss (LOH) by BAC aCGH	
Ca14007	Primary Tumor	3171ins5	fs>1025X		Positive		Normal CN by BAC aCGH	
Ca16730	Primary Tumor	1806C>T	Q563X		Loss (Null)			3b
Ca17290	Primary Tumor	IVS16+6T>G	cryptic splice activator		Loss			
1-BB	Primary Tumor	185delAG	fs>39X	WT	Positive			
3R-BB [b]	Primary Tumor	4446C>T	R1443X	WT	Loss			
3L-BB [b]	Primary Tumor	4446C>T	R1443X		Positive			
4-BB	Primary Tumor	309T>G	C64G	WT	Loss			
5-BB	Primary Tumor	5382insC	fs>1829X	WT	Loss (Null)			
6-BB	Primary Tumor	5382insC	fs>1829X	WT	Loss (Null)			
7-BB	Primary Tumor	5382insC	fs>1829X	WT	Loss (Null)			
9-BB	Primary Tumor	185delAG	fs>39X	WT	Loss			
10-BB	Primary Tumor	2594delC	fs>845X	WT	Positive			
11-BB	Primary Tumor	5382insC	fs>1829X	WT	Loss			
12-BB	Primary Tumor	309T>G	C64G	WT	Loss (Null)			
P1225	Primary Tumor	300T>G	C61G		Loss (Null)			3a
P18004	Primary Tumor	3127delTT	fs>1003X		Loss (Null)			
P5842	Primary Tumor	3171ins5	fs>1025X		Loss			
MX-1 (Bx11)	Xenograft	2795del4	fs>999X	Homozygous Deletion		Yes	Homozygous Deletion by Agilent HD-aCGH / Homozygous Deletion by BAC aCGH	SF 1a
HCC-1937	Cell Line	5382insC	fs>1829X	Homozygous Deletion	Null (WB)	Yes	Homozygous Deletion by BAC aCGH	
MDA-MB-436	Cell Line	5396+1G>A	splice donor	WT	Null (WB)	Yes	Intragenic Inversion by SP-FISH / Micro-CNI by Agilent HD-aCGH / CN Loss (LOH) by BAC aCGH	4a,d
SUM-149	Cell Line	2288delT	fs>735X	WT	Null (WB)	Yes	Intragenic Inversion by SP-FISH / Micro-CNI by Agilent HD-aCGH / CN Loss (LOH) by BAC aCGH	4b,d

[a]Patient is a member of a BRCA1 family with the IVS17-2A>C mutation, however this mutation has not been confirmed to be present in this patient. [b]3R-BB and 3L-BB are specimens from the right and left breasts from a patient with bilateral disease. The following abbreviations are used: AA, amino acid; BAC aCGH, 32K BAC array comparative genomic hybridization; CN, DNA copy number; CNI, DNA copy number increase; GPM, gross PTEN mutation; HD-aCGH, high-density aCGH; IHC, immunohistochemistry; LN, lymph node; LOH, loss of heterozygosity; SF, supplementary figure; SP-FISH, split-probe fluorescent in situ hybridization; WB, western blot; blank cell, not tested. PTEN IHC is scored for the cytoplasmic compartment relative to non-neoplastic control epithelial or stromal cells within the tissue section; complete lack of tumor cell immunodecoration is designated 'Null'.



Supplementary Figure 1
High-density oligo-aCGH analyses of (**a**) MX-1 xenograft with known *PTEN* homozygous deletion and (**b**,**c**) two PTEN$^{IHC\text{-}null}$ BRCA1-hereditary breast tumors without obvious gross *PTEN* mutation.