Figure S1

A

B

relative tumor size

0 20 40 60 80

days

0 2 04 06 08

days

T7* control

T7* docetaxel

T7* doxorubicin

T7* cisplatin
The graphs illustrate the relative tumor size over days for different treatments in two separate experiments labeled T14* and T15*.

- **T14* control**: Black line.
- **T14* docetaxel**: Light blue line.
- **T14* doxorubicin**: Red line.
- **T14* cisplatin**: Green line.

- **T15* control**: Black line.
- **T15* docetaxel**: Light blue line.
- **T15* doxorubicin**: Red line.
- **T15* cisplatin**: Green line.
T32* control  
T32* docetaxel  
T32* doxorubicin  
T32* cisplatin

T33* control  
T33* docetaxel  
T33* doxorubicin  
T33* cisplatin

days
relative tumor size

T32* and T33* tumor growth over 120 days. T32* and T33* were treated with control, docetaxel, doxorubicin, or cisplatin.
The graphs show the relative tumor size over time for different treatment conditions:

- **T40**
  - Control
  - Docetaxel
  - Doxorubicin
  - Cisplatin

- **T41**
  - Control
  - Docetaxel
  - Doxorubicin
  - Cisplatin
relative tumor size

days

T42* control
T42* doxorubicin
T42* cisplatin
T42* docetaxel

T43* control
T43* doxorubicin
T43* cisplatin
T43* docetaxel
Figure S1. Response of BRCA1;p53-deficient tumors to the maximum tolerable dose of docetaxel, doxorubicin or cisplatin. A, 6 individual K14cre,Brca1f/f,p53f/f animals carrying a spontaneous mammary tumor of ~200 mm³ (T1-T6) were treated with 25 mg docetaxel per kg mouse i.v. on days 0, 7 and 14 (arrows). When tumors relapsed back to ~200 mm³ or showed progressive growth (tumor size ≥ 50%) after a recovery time of 7 days following the day 14 injection, treatment was resumed as indicated by the filled squares. Animals carrying T2 or T4 had to be sacrificed before full docetaxel resistance developed due to the presence of a squamous cell carcinoma of the lip (T2) or ear (T4). B, animals with 37 individual orthotopically transplanted BRCA1;p53-deficient mammary tumors (volume ~200 mm³) were left untreated (black line) or treated with 25 mg docetaxel per kg i.v. on days 0, 7 and 14 (blue line), 5 mg doxorubicin per kg i.v. on day 0 (blue line), or 6 mg cisplatin per kg i.v. on day 0 (green line). When tumors relapsed or showed progressive growth (tumor size ≥ 50%) after a recovery time of 7 days (docetaxel, doxorubicin) or 14 days (cisplatin), treatment was resumed as indicated by the filled squares. The responses of T1, T3, T7, T10, T11 and T14 have already been published in Rottenberg et al. PNAS 104:12117-22, 2007.
Figure S2. Unsupervised hierarchical cluster analysis (average linkage) of gene expression data generated using the MEEBO or Illumina platform. (A) Tumors with good docetaxel response (as defined in Figure 2A) are in red, those with a poor response in green.
**Figure S3.**

A, Unsupervised hierarchical cluster analysis of gene expression data of 15 tumors that were initially sensitive to docetaxel and eventually acquired resistance. MEEBO microarrays were used to analyze untreated tumors before treatment (sensitive, red) and the corresponding resistant (green) tumors. B, HE stainings of T20*con, T20*doce-res, T38*con and T38*doce-res carcinomas. For T20*con and T38*con dense lobules of undifferentiated polyploid tumor cells separated by a fine-vascular stroma can be seen. In contrast, T20*doce-res and T38*doce-res show islands of tumor cells (arrows) separated by a thick stroma (star) containing macrophages, collagen-producing fibroblasts, lymphocytes, plasma cells and some neutrophils. Bar represents 100µm.
Figure S4. SAM of docetaxel-resistant tumors with increased Abcb1 expression by RT-MLPA (see Figure 3C). (A) Comparison of T18*con, T20*con, T22*con, T24*con, T31*con and T34*con versus T18*doce-sens, T20*doce-sens, T22*doce-sens, T24*doce-sens, T31*doce-sens and T34*doce-sens. $\Delta=1.0$, FDR=0. (B) Comparison of T6*con, T18*con, T20*con, T22*con, T24*con, T28*con, T29*con, T31*con, T34*con and T38*con versus T6*doce-sens, T18*doce-sens, T20*doce-sens, T22*doce-sens, T24*doce-sens, T28*doce-sens, T29*doce-sens, T31*doce-sens T34*doce-sens and T38*doce-sens. $\Delta=1.0$. (C) SAM (MEEBO platform) of T8*con, T9*con, T15*con, T26*con and T41*con versus the drug-naive samples of the 21 docetaxel-sensitive controls (T2, T4, T5, T6, T12*con, T17*con, T18*con, T21*con, T22*con, T24*con, T25*con, T28*con, T29*con, T30*con, T31*con, T32*con, T34*con, T35*con, T38*con, T42*con, T43*con). $\Delta=1.3$, number of significant genes=220, FDR=0.6%. (D) SAM of the same samples as shown in panel (C), but analyzed on the Illumina platform. $\Delta=1.7$, number of significant genes=91, FDR=0.9%.
Figure S5. Heatmap of the top 50 genes that correlate with the Xist expression pattern using the Illumina platform (r > 0.53).
Figure S6. Quantification of the expression of the human *XIST* gene using two independent probes. RT-MLPA analyses of a pool of RNA isolated from FFPE normal breast tissue of 8 different patients. The XIST gene expression levels were normalized to the internal reference genes present in the RT-MLPA mix (*LDHA*, 2 probes for *GAPDH*, *B2M*, *ARHGDIA*, *FAU*, *OAZ1* and *BIRC2*). Depicted is the average gene expression of 8 independent measurements (one measurement is the average of 3 independent MLPA reactions); the error bars indicate the standard deviation of these 8 measurements; the dashed line represent two times the standard deviation and was used as the cut-off for further analyses.
Figure S7. Distribution of gene expression levels of untreated KB1P mouse tumors using the probes for *Xist* or *Abcb1b* present on the MEEBO and Illumina platforms. *P* values were determined by the Kruskal-Wallis and post-hoc Mann-Whitney U tests (*Xist* probes, highest *P* value shown) or the Mann-Whitney U test only (*Abcb1b*).