**Supplementary table 1**

**1.1 shRNA sequences (5’ -> 3’)**

**shUSP11\_1:**

CCCTCCCTTCCGGCCCTCCCTTCTAGTCTTTATTCTCGAGAATAAAGACTAGAAGGGAGGGTTTTT

**shUSP11\_2:**

CCGTGATGCCGGCCGTGATGATATCTTCGTCTACTCGAGTAGACGAAGATATCATCACGGTTTTT

**shUSP11\_3:**

CCGATTCTTCCGGCCGATTCTATTGGCCTAGTATCTCGAGATACTAGGCCAATAGAATCGGTTTTT

**shUSP11\_4:**

CCGTGACTCCGGCCGTGACTACAACAACTCCTACTCGAGTAGGAGTTGTTGTAGTCACGGTTTTT

**shUSP11\_5:**

CGGCACAACCGGCGGCACAATGATTTGGGCAAACTCGAGTTTGCCAAATCATTGTGCCGTTTTT

**1.2 USP11 siRNA sequences (5’ -> 3’)**

**siUSP11\_1:**

GGACCGUGAUGAUAUCUUC

**siUSP11\_2:**

GAAGAAGCGUUACUAUGAC

**1.3 Primer sequences used in qRT-PCR analysis (5’ -> 3’):**

**USP11**

Forward: CATTGAACGCAAGGTCATAGAGC

Reverse: AGTTCTACTGGGTACACTTCGAC

**PgR**

Forward: GACACCTTGCCTGAAGTTTCG

Reverse: CTGCGTCTTTTCGTCGGAG

**TFF1**

Forward: CCCTCCCAGTGTGCAAATAAG

Reverse: GAACGGTGTCGTCGAAACAG

**ERα**

Forward: ACAAGGGAAGTATGGCTATGGA

Reverse: GGTCTTTTCGTATCCCACCTTTC

**GAPDH**

Forward: ATGGGGGAAGGTGAAGGTCG

Reverse: GGGGTCATTGATGGCAACAAT

**GREB1**

Forward: ACCAGCTTCAGTCACCTTTC

Reverse: GGAAGTTCCCATGGCCTTTA

**PKIB**

Forward: GGGACAGGAAAGATAGGAGAAAG

Reverse: CAGACTCCACGTCAGTCATTT

**TOP2A**

Forward: GCTGGATCAGTGGCTGAAAT

Reverse: ATGGGCTGCAAGAGGTTTAG

**BRCA1**

Forward: CTCGCTGAGACTTCCTGGAC

Reverse: TACCCAGAGCAGAGGGTGAA

**BLM**

Forward: CCTCTACCCAACACCACAAA

Reverse: CCTTCGGAGTCTGCAAGAAA

**TRIM22**

Forward: ACGAGGTGGTCAAGGAATGT

Reverse: CTTCTGTCTCTCGATCTGGATATAA

**IFIT1**

Forward: GAGGAGCCTGGCTAAGCAAA

Reverse: GCTCCAGACTATCCTTGACCTG

**Supplementary figure legends**

**Supplementary Figure 1**: A search for protein-protein interactions using the online database STRING revealed several putative and known interactions between ERα and the USP11 ubiquitinome.

**Supplementary Figure 2: (A, B)** PCA plots demonstrating variance between each group and replicate in **(A)** LCC1 and **(B)** LCC9 cell lines. Reads were corrected for batch effect. **(C, D)** Bar graph portraying the 10 most significant GO pathways associated with upregulated genes in **(C)** LCC1 USP11 knockdown cells and **(D)** LCC9 USP11 knockdown cells. \*\*\*\* p< 0.0001, Benjamini adjusted (FDR).

**Supplementary Figure 3:** We examined ERα-positive, breast cancer patients in The Cancer Genome Atlas (TCGA) dataset and found that one-third (n= 102) of genes in the Dutertre dataset significantly correlated with USP11 in these patients. Of the genes associated with the Dutertre gene set in LCC1 USP11 knockdown samples, 26 positively correlated with USP11 in TCGA samples. RNA-Sequencing samples of TCGA breast cancer patients were downloaded from gcd portal on the 22.Jan 2019. Correlations between USP11 and other genes were calculated based on fragments per kilobase million (FPKM) using the cor function (method = "pearson") from the stats package in R (3.6.3). Significance of correlations were determined using cor.mtest function form the corrplot package (version 0.84). Geneset overlaps were visualised using the UpSet function from the ComplexHeatmap package (2.2.0).

**Supplementary Figure 4.** IGV views of input DNA and estrogen receptor (ERα) binding in ZR751 breast cancer cells at USP11 and TFF1 genes. ChIP-seq data analysed from ArrayExpress number E-MTAB-223 (1-2). Input DNA and ERα occupancy across USP11 and TFF1 in ZR751 cells, similar binding patterns are seen in both ERα+ve MCF7 and T47D cell lines. (TFF1 is used as a positive control to show ERα binding) (1).

Methods: Analysis of sequenced ZR751, T47D and MCF7 ChIP DNA (1-2) was carried out following nf-core/chipseq pipeline (3). In brief quality control was carried using FastQC (4). Sequencing adaptors were removed using Trim galore. Trimmed reads were aligned (BWA) (5). Picard tools (MIT) mark duplicates with standard parameter settings and remove likely duplicates (6). Alignments were merged to hg38 reference genome. Reads aligning to multiple locations were excluded. Bigwig tracks uploaded to IGV (7).

References:

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