

Supplementary Figure 1

Disease	Cell line	Mutated protein	Label in Figure 1:	Affected Pathway	GGRd
None	BJ1	None	BJ1	None	No
CS	GM08156	CSB	CSB1	TCR	No
CS	GM00739	CSA	CSA	TCR	No
CS	GM01629	CSB	CSB2	TCR	No
TTD	GM15752	XPD	TTD	TFIIH, transcription	No
XPV	GM03053	POL Eta	XPV1	TLS	No
XPV	GM02359	POL Eta	XPV2	TLS	No
TTD	GM15753	XPD	TTD2	TFIIH, transcription	No
XP	GM14930	XPG	XPG	GGR and TCR	Yes
XP	GM01389	DDB2	XPE	GGR	Yes
XP	GM21071	XPB	XPB	GGR and TCR	Yes
XP	GM01630	XPA	XPA	GGR and TCR	Yes
XP	GM08207	XPD	XPD1	GGR and TCR	Yes
XP	GM03248	XPD	XPD2	GGR and TCR	Yes
XP	GM08437	XPF	XPF	GGR and TCR	Yes
XP	GM14867	XPC	XPC	GGR	Yes

Supplementary Figure 1: XP, CS, and TTD cell lines

Immortalized fibroblast cell lines from patients with Cockayne syndrome (CS), trichothiodystrophy (TTD), or xeroderma pigmentosum (XP) were subjected to NER profiling with the DDB2 proteo-probe assay. Each cell line has bi-allelic loss or mutation of a specific gene in the NER pathway; however, only patients with loss of a gene in the global genome repair (GGR) sub-pathway of NER exhibit a DNA repair deficient phenotype in the DDB2 proteo-probe assay. Loss of a gene involved in transcription (TFIIH), translesion synthesis (TLS), or transcription-coupled repair (TCR) do not exhibit a NER deficient phenotype in the DDB2 proteo-probe assay. BJ1 is a normal human fibroblast cell line without any NER defects. TCR: transcription-coupled repair; GGR: global genome repair; TFIIH: transcription factor IIH; TLS: trans-lesion synthesis; GGRd: deficient in global-genome sub-pathway (or the common/shared nucleotide excision repair pathway).

Supplementary Figure 2

Cell line	ER	PR	HER2
AU565	-	-	+
BT20	-	-	
BT474	+	+	+
BT549	-	-	
CAMA-1	+	-	
HCC38	-	-	
HCC70	-	-	
HCC202	-	-	+
HCC1143	-	-	
HCC1187	-	-	
HCC1395*	-	-	
HCC1419*	-	-	+
HCC1428	+	+	
HCC1500	-	-	
HCC1569	-	-	+
HCC1806*	-	-	
HCC1954	-	-	+
Hs578T	-	-	
MCF7	+	+	
MDA-Kb2**	-	-	
MDA-MB-157	-	-	
MDA-MB-175-VII	+	-	
MDA-MB-231	-	-	
MDA-MB-361	+	-	+
MDA-MB-436	-	-	
MDA-MB-453	-	-	
MDA-MB-468	-	-	
SK-BR-3	-	-	+
SUM149	-	-	
SUM1315	-	-	
T47D	+	+	
UACC-812	+	-	+
UACC-893*	-	-	+
ZR-75-1	+	-	
ZR-75-30	+	-	+

Supplementary Figure 2. Breast cancer cell lines

For each breast cancer cell line in this study, the ER, PR, and HER2 status is shown based on data from Neve et al[32]. Cell lines not included in the Neve et al study are denoted with asterisks; for these lines, receptor status was obtained from the ATCC website. ER, PR, and HER2 status for MD-Kb2 were not available; therefore, data from MDA-MB-453 (the parental line for MD-Kb2) are shown.

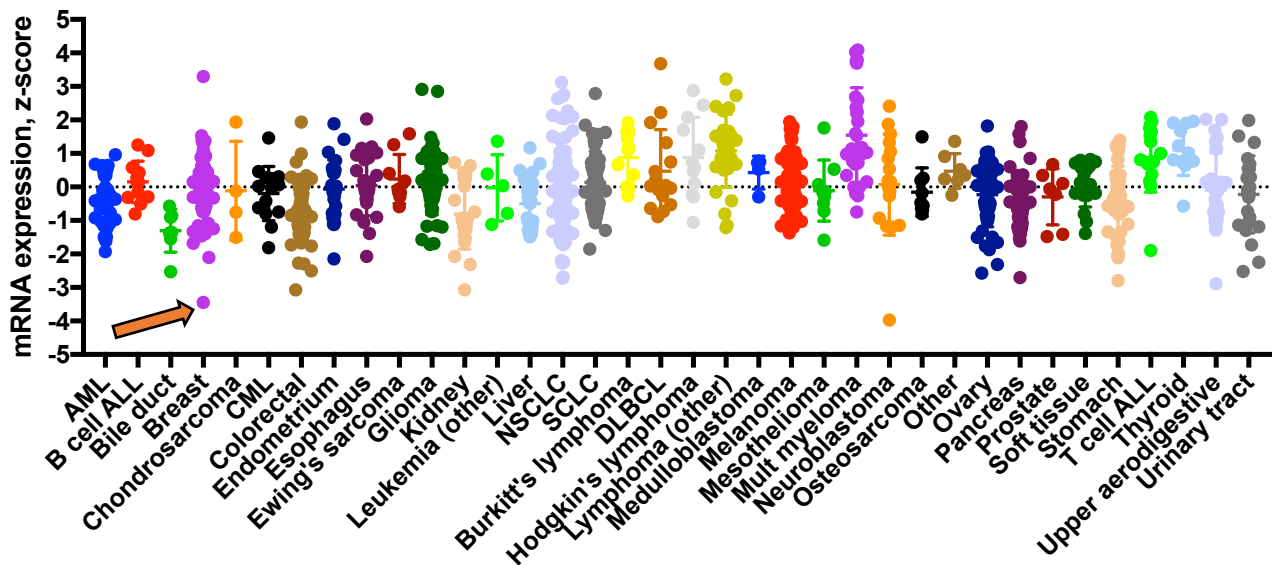
Supplementary Figure 3

Gene	Protein	Pathway
DDB1	DDB1 / XPE	GGR
DDB2	DDB2 / XPE	
XPC	XPC	
ERCC6	CSB	TCR
ERCC8	CSA	
XAB2	XAB2	Both
CCNH	Cyclin H	
CDK7	Cdk7	
CETN2	Centrin-2	
CUL4A	Culin 4A	
ERCC1	ERCC1	
ERCC2	ERCC2 / XPD	
ERCC3	ERCC3 / XPB	
ERCC4	ERCC4 / XPF	
ERCC5	ERCC5 / XPG	
GTF2H1	GTF2H1	
GTF2H2	GTF2H2	
GTF2H3	GTF2H3	
GTF2H4	GTF2H4	
GTF2H5	GTF2H5	
MMS19	MMS19	
MNAT1	MNAT1	
NEDD8	NEDD8	
RAD23A	RAD23A	
RAD23B	RAD23B	
RBX1	Roc1	
RNF111	RNF111	
RPA1	RPA1 / RPA70	
RPA2	RPA2 / RPA32	
RPA3	RPA3	
UBE2I	Ubc9	
USP7	USP7	
XPA	XPA	

Supplementary Figure 3: Nucleotide excision repair (NER) gene set list.

GGR, global genome repair sub-pathway; TCR, transcription-coupled repair sub-pathway.

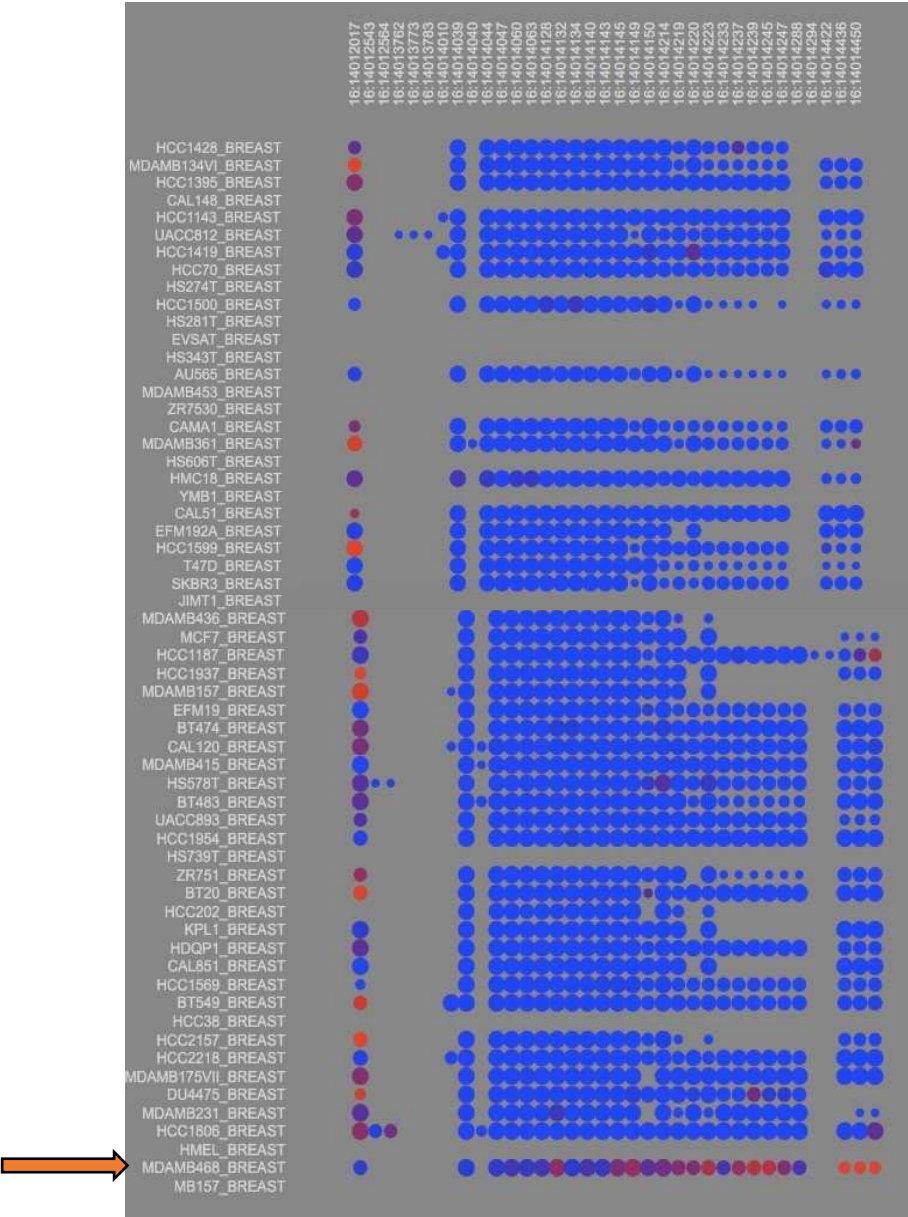
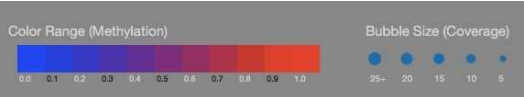
Supplementary Figure 4



Supplementary Figure 4: *ERCC4* mRNA expression levels across cell lines from the Cancer Cell Line Encyclopedia (CCLE).

MDA-MB-468 (denoted by orange arrow) has the lowest *ERCC4* expression across breast cancer cell lines and the second lowest *ERCC4* expression across all cancer cell lines. Data was downloaded from the CCLE website (<https://portals.broadinstitute.org/ccle>) and plotted using Prism (GraphPad).

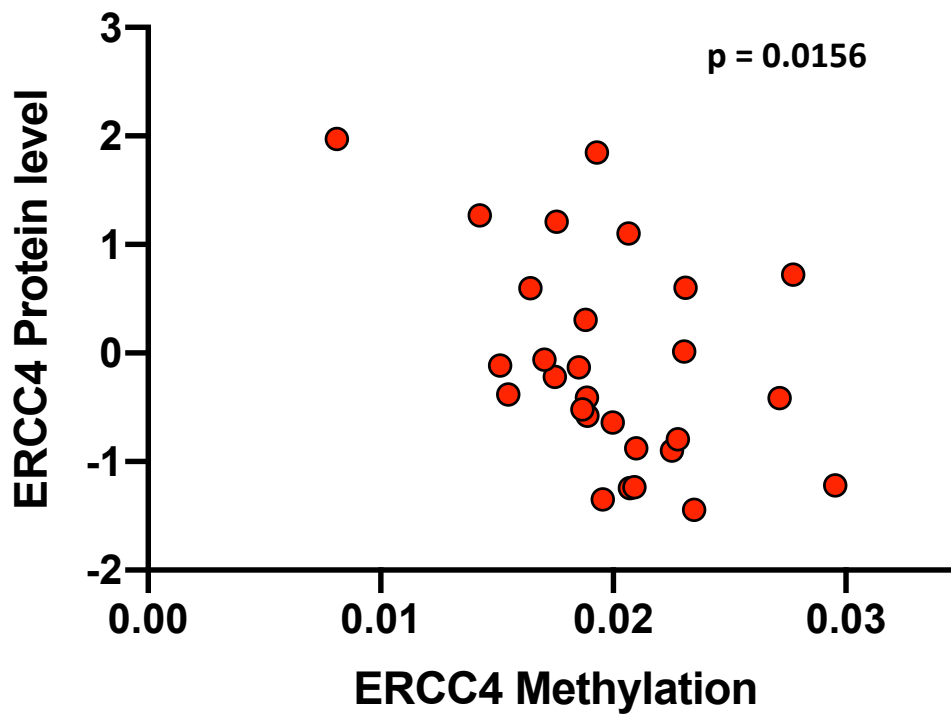
Supplementary Figure 5



Supplementary Figure 5: CpG methylation of the *ERCC4* gene.

ERCC4 gene methylation from all available breast cancer cell lines in the Cancer Cell Line Encyclopedia (CCLE). MDA-MB-468 (denoted by orange arrow) has the highest levels of *ERCC4* methylation among all lines.

Supplementary Figure 6



Supplementary Figure 6: Correlation between *ERCC4* gene methylation and XPF protein levels.

Data from the breast cancer TCGA cohort were downloaded via the cBioPortal interface (www.cbioportal.org) and figures were generated using Prism (GraphPad).