Supplementary Table 1. Clinical Characteristics & Demographics (5).

Age	
Mean (SD)	71.3 (8.26)
Median	70.0
Range	(56.0-87.0)
HER 2	
Missing	16
0	16
1	5
2	1
3	7
T Stage	
T2	35 (77.8%)
T3	3 (6.7%)
T4	6 (13.3%)
T4b	1 (2.2%)
Aromatase Inhibitor	
Anastrozole	21 (46.7%)
Exemestane	10 (22.2%)
Letrozole	14 (31.1%)

Supplementary Table 2. *CYP19* Resequencing Primers				
	Forward (F) or Reverse (R)	**M13 Tag Sequence**	**Primer Sequence**	**T_a(C)**
Exon 1.1	F		CCAACAAAAGCACAAAGGAAA	64
	R		TATCCAGCACACAACATCAGC	
Exon 2a	F		TAAAAATGAAGCTGCCACTCTCT	58
	R		TTATGGTCTTAAGCATGGCTTTG	
Exon 1.4	F		TGAAGGGAGAATAATTGGGAAC	58
	R		GGTAGCCTAAGCCGTCCTTC	
Exon 1.5	F		CCCTCTTCTTTTCCGAGGTG	63
	R		CCCGAATCTTGACATTTGCT	
Exon 1.7	F		GCCCTCTCCTTTCTCAGGAC	57
	R		TGTCACTTCGAAAGGGGCTAC	
Exon 1.f	F	TGTAAAACGACGGCCAGT	GGTTCTGCTTTGCAACTTCTCT	55
	R	CAGGAAACAGCTATGACC	GAACGATGCAACCTGTTGGT	
Exon 1.2	F	TGTAAAACGACGGCCAGT	ACCCTTTTTCCTGGGGAGTT	55
	R		ACTCCCCGAGGCTAATAAAAGT	
Exon 1.6 Exon 1.3 Exon 2	F		ATATTTCCCTCCTGCTCCTTCT	55
	R	CAGGAAACAGCTATGACC	ATTACGGTTACAGGGGGTCTTT	
Exon 3	F	TGTAAAACGACGGCCAGT	TTCATTTAACAAGCTGCCTCTTACT	55
	R		AGCACATGAATCTTTAGAGAACACA	
Exon 4	F		GCACTTGAAGCCAGAGTTCAC	57
	R	CAGGAAACAGCTATGACC	CCCTCCTCTCCCCTCTTAACT	
Exon 5	F		CAATACCTGTGGGTGTCTTGG	55
	R		TTCCCATTTTTATTGGGCAGT	
Exon 6	F		TTGAATAAACTGTGTAGCGCAGA	56
	R		CACCTGTATTCACCTGACTCTCC	
Exon 7 Exon 8	F		AAAAACACAAGAGGGTTTGTGAGT	55
	R		TCTATTTCCAGTTTGCCTAGATCC	
Exon 9	F		CCAAGATGCAGGAAGTTTAAGG	56
	R		TGGTGTCACTTACTGTGCCTTT	
Exon 10	F		ATCCCAACCCAAACTGTTGA	59
	R		TCCTGAAGCAGGGGTAACTC	

<u>Supplementary Table 3</u>. Primers for site-direct mutagenesis and EMSA probes. Nucleotides that are underlined represent the restriction enzyme site. SNPs are highlighted for site-directed mutagenesis and for EMSA probes.

Site-directed mutagenesis His (128)Arg, (A->G; CAT->CGT) **Primer Sense:** 5'-AGTGCATCGGTATGC**G**TGAGAAAGGCATCAT Primer Anti-sense: 5'-ATGATGCCTTTCTCA**C**GCATACCGATGCACT Reporter gene constructs: **Primer Sense: gtca <u>acgcgt</u>** GACTGATCAT CTCTCAGCAA TACCCAC **Primer Anti-sense: catg <u>ctcgag</u>** CCAACACTATCTACCTGGAAAGAGT EMS Assay Probes (-588, -144)
P1.1 -588 wild-type Sense: 5'-TCA CTA TTA CCC **G**TT GAA TAA ATG AG
P1.1 -588 wild-type Anti-sense: 5'-CTC ATT TAT TCA A**C**G GGT AAT AGT GA
P1.1 -588 A variant Sense: 5'-TCA CTA TTA CCC **A**TT GAA TAA ATG AG
P1.1 -588 A variant Anti-sense: 5'-CTC ATT TAT TCA A**T**G GGT AAT AGT GA
P1.1 -144 wild-type Sense: 5'-AGT CAT GGA CAA **C**AA ATG AAA TCTC
P1.1 -144 wild-type Anti-sense: 5'-GAG ATT TCA TTT **G**TT GTC CAT GACT
P1.1 -144 T-variant Sense: 5'-AGT CAT GGA CAA **T**AA ATG AAA TCTC
P1.1 -144 T-variant Anti-sense: 5'GAG ATT TCA TTT **A**TT GTC CAT GACT

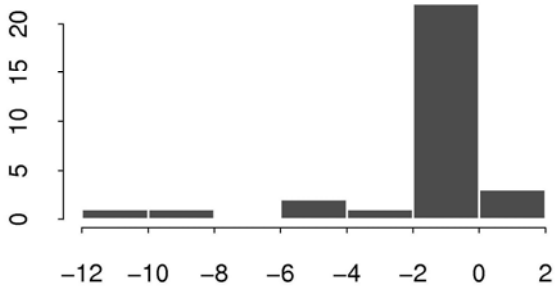
Location	Nucleotide	Sequence Change	Amino Acid Change	Coriell Caucasian n=60	Edinburgh Tissue Samples (tumor and normal) n=52
5'FR Exon I.1	**-588**	**G→A**		**0.142**	0.154
5'FR Exon I.1	-245	G→T		0.008	0.000
5'FR Exon I.1	**-144**	**C→T**		**0.158**	0.154
5'FR Exon 2a	-639	G→A		0.008	0.000
5'FR Exon 2a	-602	C→T		0.000	0.010
5'FR Exon 2a	**-468**	**C→T**		**0.175**	0.125
5'FR Exon 2a	-429	T→C		0.042	0.029
Exon 2a	-21	C→A		0.008	0.000
5'FR Exon I.5	**-628**	**C→G**		**0.867**	0.192
5'FR Exon I.5	**-334**	**T→C**		**0.050**	0.029
5'FR Exon I.5	**-317**	**G→C**		**0.092**	0.154
5'FR Exon I.7	***-1051***	***deletion of CTTT***		***0.092***	0.154
5'FR Exon I.7	***-1000***	***deletion of CTT***		***0.010***	0.063
5'FR Exon I.7	***-787***	***C→T***		***0.104***	0.026
5'FR Exon I.7	***-734***	***A→G***		***0.008***	0.010
5'FR Exon I.7	-439	A→C		0.008	0.010
Intron I.7	**54**	**G→C**		**0.058**	0.038
Intron I.7	***57***	***Deletion of TC***		***0.008***	0.010
5'FR Exon I.f	-725	G→A		0.092	0.135
5'FR Exon I.f	-690	A→C		0.092	0.135
5'FR Exon I.f	**-649**	**C→T**		**0.942**	0.923
Exon I.f	-64	C→T		0.000	0.019
Exon I.f	-35	A→G		0.000	0.019
5'FR Exon I.2	-827	A→G		0.000	0.010
5'FR Exon I.2	**-596**	**T→C**		**0.125**	0.163

Exon I.2	**-224**	**G→C**		**0.450**	0.490
5'FR Exon I.6	-273	T→A		0.008	0.000
5'FR Exon I.6	**-196**	**A→C**		**0.608**	0.423
Exon I.6	**-77**	**G→A**		**0.117**	0.490
Intron I.6	61	C→T		0.025	0.087
Exon PII	-83	C→A		0.008	0.000
Intron 2	**-59**	**A→G**		**0.542**	0.442
Exon 3	186	C→T		0.008	0.000
Exon 3	**240**	**A→G**		**0.542**	0.442
Intron 3	***-76***	***A→G***		0.317	0.442
Exon 4	383	A→G	His (128) Arg	0.000	0.010
Intron 4	**27**	**TCT I→D**		**0.333**	0.337
Exon 5	602	C→T	Thr (201) Met	0.050	0.048
Intron 5	**-16**	**T→G**		**0.542**	0.433
Intron 6	**36**	**A→T**		**0.542**	0.433
Intron 6	**-106**	**T→G**		**0.542**	0.442
Exon 7	**790**	**C→T**	**Arg (264) Cys**	**0.025**	0.029
Intron 7	**26**	**C→T**		**0.100**	0.067
Intron 7	***101***	***deletion of T***		***0.025***	0.019
Intron 7	***106***	***A→G***		***0.033***	0.029
Intron 7	***118***	***A→C***		***0.500***	0.442
Intron 7	***290***	***G→A***		***0.025***	0.038
Intron 7	**-79**	**A→G**		**0.542**	0.442

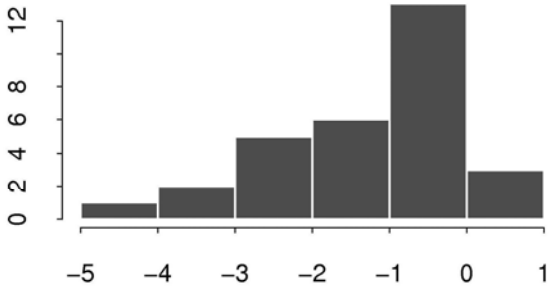
Intron 8	***-53***	***T→G***		***0.525***	0.442
3'UTR	1527	T→C		0.000	0.010
3'UTR	**1531**	**C→T**		**0.558**	0.442
3'UTR	**1673**	**G→T**		**0.292**	0.212

Supplementary Table 4. Human *CYP19* gene resequencing. Locations of polymorphisms, alterations in nucleotide and amino acid sequences, as well as observed minor allele frequencies for each SNP are listed. The numbering of polymorphisms in individual noncoding exon 1s and upstream 5'-FRs is based on their distance from the 3'-splice junction for that exon. Negative or positive numbers are located 5' or 3' to this position, respectively. Letters represent individual upstream noncoding exons. Numbering of polymorphisms in coding exons 2-10 and downstream of the 3'-UTR begins from the "A" in the translation initiation codon in exon 2. Variant nucleotides in introns are numbered based on their distance to the nearest splice site, with positive numbers for 3' and negative numbers for 5' splice site. Rs numbers are listed when they have been assigned. Those SNPs present in dbSNP are "highlighted". SNPs identified during the present resequencing study using Coriell DNA samples are italicized.

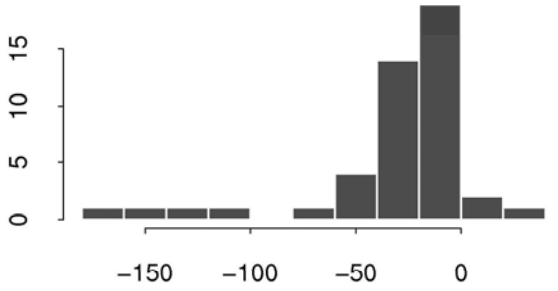
<u>Supplementary Figure 1</u>. Distribution of phenotypes for breast cancer patients. These phenotypes were described in a previous study (5).



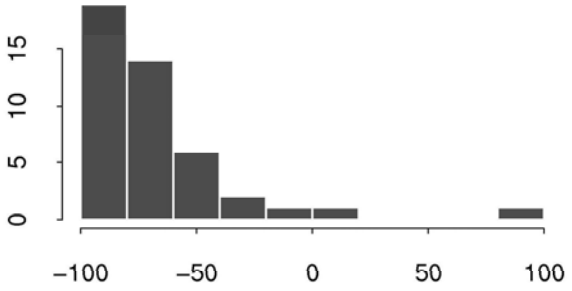
Post-Pre E1 (pmol/gm)



Post-Pre E2 (pmol/gm)



Aromatase, % change with treatment



Tumor Size, % change with treatment

<u>Supplementary Figure 2</u>. *CYP19* Linkage Disequilibrium Plot. LD within the area of *CYP19* resequenced, shown as pairwise r^2 values, is depicted graphically. The darker the color, the higher the LD between the two SNPs.