

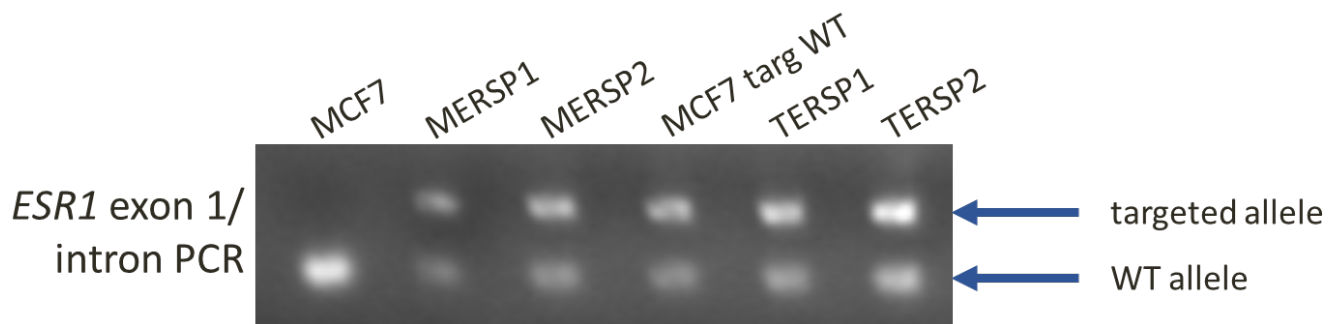
**SUPPLEMENTAL MATERIALS**  
**Supplemental Tables S1 and S1**  
**Supplemental Figure S1**

Source	Population	Variant Allele Count	Total Allele Count	Allele Frequency	
Exome Aggregation Consortium (ExAC)		312	31964	.0098	*2 homozygotes
	Finnish	55	708	.0777	
	European (non-Finnish)	222	17332	.0128	*2 homozygotes
	Latino	25	2288	.0109	
	African	5	2402	.0021	
	South Asian	5	6288	.0007	
	East Asian	0	2746	0	
	Other	0	200	0	
Exome Variant Server (GO-ESP)		31	12278	.0025	*0 homozygotes
	European American	27	8156	.0033	
	African American	4	4122	.0010	
Atherosclerosis Risk in Communities		44	15726	.0028	
	European American	40	10230	.0039	
	African American	4	5496	.0007	
TOPMed		78		.0027	
1000 Genomes		8		.0016	

**Supplemental Table S1: ER S118P variant allele frequency in the general population categorized by population.** Data from Table 1 subcategorized by demographic populations.

Variable	Cancer-free (N=268)	BC survivors (N=268)
Age at baseline, years, mean (SD)	50.1 (11.2)	50.6 (11.3)
Postmenopausal, %	44.4	60.4
Age at menopause, years, mean (SD)	49.7 (6.3)	48.9 (5.4)
BMI, kg/m <sup>2</sup> , mean (SD)	27.0 (6.6)	26.2 (5.6)
Physical activity, mean MET-h/week (SD) <sup>a</sup>	27.4 (31.8)	26.7 (30.3)
Smoking, %		
Never	58.6	54.9
Former	36.2	40.3
Current	4.5	4.5
Missing	0.7	0.4
Alcohol intake, mean (SD)	6.6 (10.3)	5.8 (10.0)
Time from diagnosis to baseline, years, mean (SD)	-	2.8 (4.2)
Age at diagnosis, years, mean (SD)	-	47.8 (10.9)
Breast cancer stage, %		
In situ	-	0.7
Stage I-III	-	96.6
Stage IV	-	2.6
ER-status, %		
Negative	-	23.9
Positive	-	75.0
Missing	-	1.1
PR-status, %		
Negative	-	31.7
Positive	-	67.2
Missing	-	1.1
HER2 status, %		
Negative	-	81.3
Positive	-	14.6
Unknown/Missing	-	4.1
Triple negative breast cancer, %	-	18.7
<sup>a</sup> Metabolic equivalents from recreational and occupational activity		

**Supplemental Table S2: Breast and Ovarian Surveillance Service (BOSS) cohort characteristics.** Cohort of individuals with a family history of breast cancer (BC).



**Figure S1:** A polymerase chain reaction using primers spanning the intronic loxP scar following *ESR1* exon 1 shows two products: the smaller band contains the wild-type sequence, while the larger band indicates targeting of one allele due to presence of the resulting 121 base pair residual sequence from the targeting construct.