

Supplementary

Table S1 The data of HTRA1 immunohistochemistry stain for normal breast tissues (antibody, HPA036655)

No.	Age (year)	Tissue type	Breast tissue type	Staining	Intensity	Quantity	Localization
1	32	Normal tissue	Adipocytes	Not detected	Negative	None	None
			Glandular cells	Not detected	Negative	None	None
			Myoepithelial cells	Not detected	Negative	None	None
2	45	Normal tissue	Adipocytes	Not detected	Negative	None	None
			Glandular cells	Not detected	Negative	None	None
			Myoepithelial cells	Not detected	Negative	None	None

HTRA1, high temperature requirement A1.

Table S2 The data of HTRA1 immunohistochemistry stain for breast cancer tissues (antibody, HPA036655)

No.	Age (year)	Type	Staining	Intensity	Quantity	Localization
1	61	Ductal carcinoma	Low	Weak	>75%	Cytoplasmic/membranous
			Low	Weak	>75%	Cytoplasmic/membranous
2	85	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
3	83	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
4	30	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
5	75	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
6	43	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
7	80	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
8	38	Ductal carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
9	40	Ductal carcinoma	Not detected	Negative	None	None
10	66	Lobular carcinoma	Low	Weak	75–25%	Cytoplasmic/membranous
			Low	Weak	75–25%	Cytoplasmic/membranous
11	59	Lobular carcinoma	Not detected	Negative	None	None
			Not detected	Negative	None	None
12	49	Lobular carcinoma	Low	Weak	Weak	Cytoplasmic/membranous
			Low	Weak	Weak	Cytoplasmic/membranous

HTRA1, high temperature requirement A1.

Table S3 Functional annotation of DEGs between BRCA groups with high- or low-*HTRA1* expression

Ontology	ID	Description	GeneRatio	P value	P _{adj}
BP	GO:0070268	Cornification	22/532	7.1761E-13	2.4463E-09
BP	GO:0019730	Antimicrobial humoral response	22/532	4.3837E-12	7.472E-09
BP	GO:0030198	Extracellular matrix organization	38/532	7.2943E-12	8.2888E-09
BP	GO:0043062	Extracellular structure organization	40/532	2.9444E-11	2.5094E-08
BP	GO:0030199	Collagen fibril organization	14/532	2.2374E-10	1.5254E-07
CC	GO:0062023	Collagen-containing extracellular matrix	42/556	3.8383E-13	1.5084E-10
CC	GO:0005581	Collagen trimer	18/556	3.0637E-11	5.7245E-09
CC	GO:0005583	Fibrillar collagen trimer	8/556	5.8265E-11	5.7245E-09
CC	GO:0098643	Banded collagen fibril	8/556	5.8265E-11	5.7245E-09
CC	GO:0000786	Nucleosome	19/556	1.4342E-10	1.1273E-08
MF	GO:0005201	Extracellular matrix structural constituent	30/518	5.8906E-16	3.4931E-13
MF	GO:0030020	Extracellular matrix structural constituent conferring tensile strength	13/518	8.3021E-11	2.4616E-08
MF	GO:0005518	Collagen binding	15/518	6.9097E-10	1.3658E-07
MF	GO:0048407	Platelet-derived growth factor binding	6/518	2.4916E-07	3.6938E-05
MF	GO:0005216	Ion channel activity	32/518	6.9698E-07	8.2662E-05
KEGG	hsa04974	Protein digestion and absorption	17/228	3.3749E-09	7.1211E-07
KEGG	hsa04742	Taste transduction	15/228	1.3389E-08	1.4126E-06
KEGG	hsa04080	Neuroactive ligand-receptor interaction	30/228	2.3175E-08	1.63E-06
KEGG	hsa05322	Systemic lupus erythematosus	16/228	1.2414E-06	6.5486E-05
KEGG	hsa05034	Alcoholism	18/228	5.0327E-06	0.00020818

DEG, differentially expressed gene; BRCA, breast cancer; HTRA1, high temperature requirement A1; BP, biological process; GO, Gene Ontology; CC, cellular component; MF, molecular function; KEGG, Kyoto Encyclopedia of Genes and Genomes.

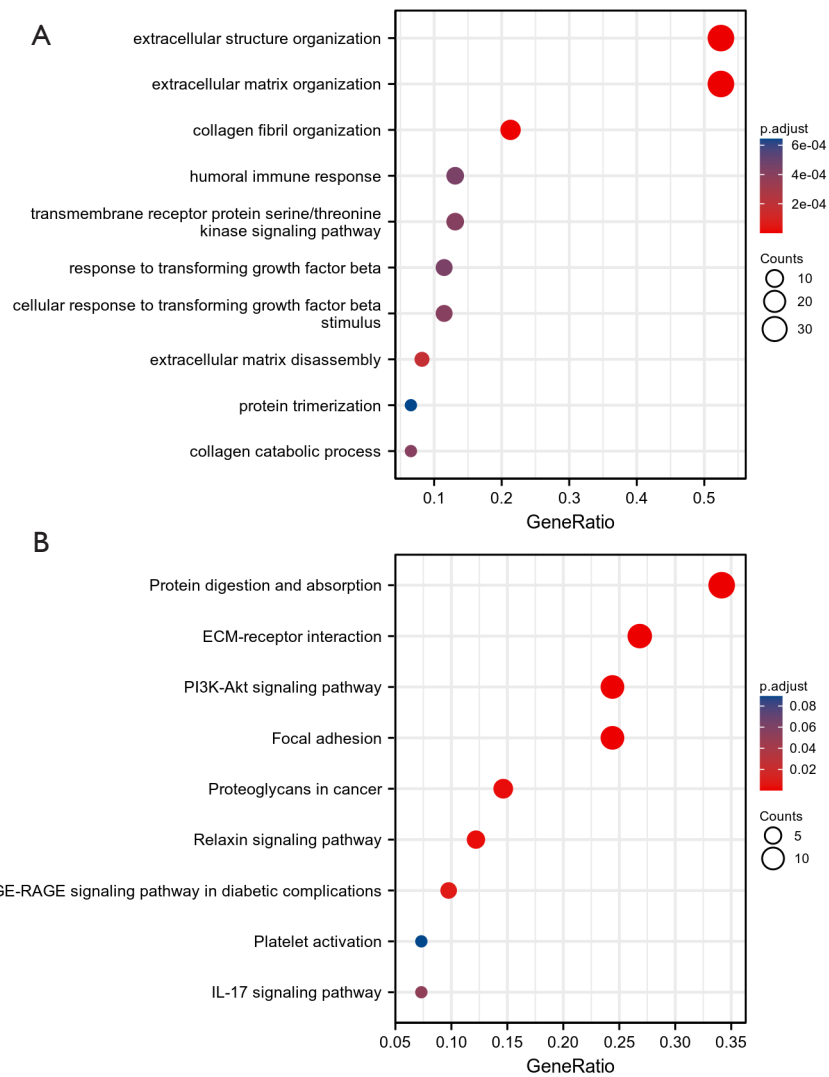


Figure S1 The enrichment results of GO BP and KEGG pathway of the DEGs interacted with *HTRA1* in *Figure 1B*. *HTRA1*, high temperature requirement A1; GO, Gene Ontology; BP, biological process; KEGG, Kyoto Encyclopedia of Genes and Genomes; DEG, differentially expressed gene.

Table S4 The correlations between *HTRA1* expression and immune cell biomarkers in BRCA

Immune cell	Biomarker	Cor	P value
B cell	CD19	0.056	0.064
	CD20 (KRT20)	0.020	0.501
	CD38	-0.078	0.010*
CD8 ⁺ T cell	CD8A	0.104	5.07E-04***
	CD8B	0.067	0.025*
TFH	BCL6	0.183	9.83E-10***
	ICOS	0.027	0.372
	CXCR5	0.049	0.105
Th1	T-bet (TBX21)	0.076	0.011*
	STAT1	-0.004	0.888
	STAT4	0.208	2.69E-12***
	IL12RB2	-0.169	1.41E-08***
	WSX1 (IL27RA)	0.057	0.057
	IFN- γ (IFNG)	-0.056	0.061
	TNF- α (TNF)	-0.029	0.327
Th2	CCR3	0.085	0.005**
	GATA3	0.134	7.53E-06***
	STAT5A	0.232	6.73E-15***
	STAT6	0.237	1.36E-15***
Th9	IRF4	0.090	0.003**
	PU.1 (SPI1)	0.295	4.87E-24***
	TGFBR2	0.599	<0.001***
Th17	IL-17A	-0.074	0.013*
	IL-21R	0.245	1.39E-16 ***
	IL-23R	0.114	1.39E-04***
	STAT3	0.207	3.64E-12***
Th22	AHR	0.310	<0.001***
	CCR10	0.343	6.37E-32***
Treg	CCR8	0.092	0.002**
	CD25 (IL2RA)	0.050	0.095
	FOXP3	0.096	0.001**
M1 macrophage	COX2 (PTGS2)	0.187	3.97E-10***
	INOS (NOS2)	0.270	6.29E-20***
	IRF5	0.036	0.229
M2 macrophage	ARG1	0.041	0.173
	CD206 (MRC1)	0.207	4.19E-12***
	CD115 (CSF1R)	0.386	<0.001***
TAM	PDCD1LG2	0.231	9.11E-15***
	CD80	0.101	7.89E-04***
	CD40	0.265	3.6E-19***

*, P<0.05; **, P<0.01; ***, P<0.001. HTRA1, high temperature requirement A1; BRCA, breast cancer; Cor, correlation; TFH, T follicular helper; Th1, type 1 Th cells; Th2, type 2 Th cells; Th9, type 9 Th cells; Th17, type 17 Th cells; Th22, type 22 Th cells; TReg, regulatory T cells; TAM, tumor-associated macrophage.

Table S5 The difference of *HTRA1* expression in breast cancer patients with or without pathological complete response to chemotherapy and anti-HER2 therapy (Mann-Whitney test)

Subtype	Number	Non-responder	Responder	AUC	ROC P value	P value	Fold change
All ^a	591	327	264	0.515	0.27	0.53	1
TNBC ^a	223	123	100	0.552	0.09	0.18	1.1
Luminal A ^a	176	84	92	0.554	0.11	0.21	1.1
Luminal B ^a	87	54	33	0.654	4.5E-03	0.016*	1.5
HER2 ⁺ ER ^{-a}	105	66	39	0.536	0.27	0.54	1.1
HER2 ⁺ ER ^{-b}	51	24	27	0.554	0.26	0.52	1.2

^a, chemotherapy; ^b, anti-HER2 therapy. *, P<0.05. HTRA1, high temperature requirement A1; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; TNBC, triple-negative breast cancer; ROC, receiver operating characteristic; AUC, area under curve.