Supplementary Tables

Title: Co-expression effect of LLGL2 and SLC7A5 to predict prognosis in ERα-positive breast cancer

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Supplementary Table S1

Association between *LLGL2* mRNA expression and clinicopathological characteristics in all breast cancer patients

	All patients	*LLGL2* mRNA expression		
		Low	High	*P* value
	n (%)	n (%)	n (%)	
Patients	624	337	287	
Menopausal status				0.46
Pre	262 (42.0)	146 (43)	116(43)	
Post	360 (57.7)	189(56)	171(57)	
Unknown	2 (0.3)	2 (1)		
Tumor size				0.047
≤2cm	240 (38.4)	117 (34.7)	123 (43)	
>2cm	383 (61.4)	219 (65.0)	164 (57)	
Unknown	1 (0.2)	1 (0.3)		
Nodal status				0.031
Negative	339 (54)	196 (58)	143 (50)	
Positive	257 (41)	125 (37)	132 (46)	
Unknown	28 (5)	16 (5)	12 (4)	
Grade				0.62
1	164 (26)	89 (27)	75 (26)	
2	191 (31)	98 (29)	93 (32)	
3	253 (41)	141 (42)	112 (39)	
Unknown	16 (3)	7 (2)	9 (3)	
Histology				0.37
IDC	556 (89)	301(89)	255 (89)	
ILC	27 (4)	9 (3)	18 (6)	
Others	41 (7)	27 (8)	14 (5)	
ERα status				0.28
Positive	491 (78.7)	259 (76.9)	232 (81)	
Negative	132 (21.1)	77 (22.8)	55 (19)	
Unknown	1 (0.2)	1 (0.3)	0 (0)	
PgR status				0.93
Positive	442 (71)	239 (71)	203 (71)	
Negative	181 (29)	97 (29)	84 (29)	
Unknown	1 (0.2)			
HER2 status				0.34
Positive	82 (13)	40 (12)	42 (15)	
Negative	518 (83)	283 (84)	235 (82)	
Unknown	24 (4)	14 (4)	10 (3)	
Adjuvant therapy				
ET alone	265 (42)	150 (45)	115 (40)	
CT alone	92 (15)	62 (18)	30 (10)	
ET+CT	206 (33)	92 (27)	114 (40)	
None	51 (8)	26 (8)	25 (9)	
Unknown	10 (2)	7 (2)	3 (1)	

ERα, estrogen receptor α; PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma;

HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; CT, chemotherapy.

Supplementary Table S2

Association between *LLGL2* mRNA expression and clinicopathological characteristics in ERα-breast cancer patients

	All patients	*LLGL2* mRNA expression		
		Low	High	*P* value
	n (%)	n (%)	n (%)	
Patients	491	259	232	
Menopausal status				0.36
Pre	216 (44)	119 (46)	97 (42)	
Post	275 (56)	140 (54)	135 (58)	
Tumor size				0.10
≤2cm	207 (42)	100 (38)	107 (46)	
>2cm	284 (58)	159 (62)	125 (54)	
Nodal status				0.007
Negative	258 (53)	151 (59)	107 (46)	
Positive	209 (43)	96 (37)	113 (49)	
Unknown	24 (4)	12 (5)	12 (5)	
Grade				0.67
1	160 (33)	87 (34)	73 (32)	
2	153 (31)	78 (30)	75 (32)	
3	166 (34)	89 (34)	77 (33)	
Unknown	12 (2)	5 (2)	7 (3)	
Histology				0.12
IDC	438 (89.2)	234 (90)	205 (88)	
ILC	26 (5.3)	9 (3)	17 (7)	
Others	26 (5.3)	16 (7)	10 (4)	
Unknown	1 (0.2)	0	0	
PgR status				0.09
Positive	426 (87)	231 (89)	195 (84)	
Negative	65 (13)	28 (11)	37 (16)	
Unknown	0	0	0	
HER2 status				0.44
Positive	45 (9)	21 (8)	24 (10)	
Negative	429 (87)	227 (88)	202 (87)	
Unknown	17 (4)	11 (4)	6 (3)	
Adjuvant therapy				
ET alone	251 (51)	141 (54)	110 (47)	
CT alone	29 (6)	22 (8)	7 (3)	
ET+CT	173 (35)	77 (30)	96 (41)	
None	32 (7)	15 (6)	17 (7)	
Unknown	7 (1)	5 (2)	2 (1)	
Endocrine therapy				
With tamoxifen	272 (56)	143 (55)	129 (56)	
Without tamoxifen	152 (31)	75 (29)	77 (33)	
None	60 (12)	36 (14)	24 (10)	
Unknown	7 (1)	5 (2)	2 (1)	

PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; CT, chemotherapy.

Supplementary Table S3

Univariate and multivariate analyses of factors associated with DFS and OS including *LLGL2* in all patients

Variate	n (%)	Univariate (DFS) *P*-value	Univariate (OS) *P*-value	Multivariate (DFS) *P*-value	HR (95% CI)	Multivariate (OS) *P*-value	HR (95% CI)
Menopausal status							
Pre	247 (44)						
Post	313 (56)	0.49	0.44				
Tumor size							
≤ 2 cm	215 (38)						1 (Reference)
> 2 cm	345 (62)	0.041	0.003			0.064	1.53 (0.98, 2.39)
Nodal status							
Negative	316 (56)				1 (Reference)		1 (Reference)
Positive	244 (44)	< 0.0001	< 0.0001	< 0.0001	3.71 (2.64, 5.22)	< 0.0001	3.70 (2.45, 5.59)
Grade							
1 and 2	323 (58)						
3	237 (42)	0.039	0.022				
Histology							
IDC	509 (91)						
ILC	19 (3)	0.93	0.67				
Others	32 (6)	0.20	0.47				
ERα status							
Positive	443 (79)				1 (Reference)		1 (Reference)
Negative	117 (21)	0.001	0.001	< 0.0001	2.18 (1.53, 3.10)	< 0.0001	2.29 (1.52, 3.45)
HER2 status							
Negative	484 (86)						
Positive	76 (14)	0.042	0.042				
LLGL2 mRNA expression							
Low	299 (53)				1 (Reference)		1 (Reference)
High	261 (47)	0.026	0.10	0.083	1.33 (0.96, 1.82)	0.17	1.30 (0.89, 1.89)

ERα, estrogen receptor α; PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2;

ET, endocrine therapy; CT, chemotherapy.

Supplementary Table S4

Univariate and multivariate analyses of factors associated with DFS and OS including *LLGL2* in ERα-positive breast cancer patients

Variate	n (%)	Univariate (DFS) P-value	Univariate (OS) P-value	Multivariate (DFS) P-value	HR (95% CI)	Multivariate (OS) P-value	HR (95% CI)
Menopausal status							
Pre	206 (46)						
Post	237 (54)	0.29	0.20				
Tumor size							
≤ 2 cm	184 (42)						1 (Reference)
> 2 cm	259 (58)	0.14	0.011			0.043	1.53 (0.98, 2.39)
Nodal status							
Negative	244 (55)				1 (Reference)		1 (Reference)
Positive	199 (45)	< 0.0001	< 0.0001	< 0.0001	3.07 (2.05, 4.61)	< 0.0001	2.90 (1.76, 4.77)
Grade							
1 and 2	287 (65)						
3	156 (35)	0.39	0.11				
Histology							
IDC	402 (91)						
ILC	18 (4)	0.6	0.37				
Others	23 (5)	0.09	0.29				
HER2 status							
Negative	402 (91)				1 (Reference)		1 (Reference)
Positive	41 (9)	0.19	0.038	0.04	1.84 (1.02, 3.29)	0.004	2.58 (1.35, 4.95)
LLGL2 mRNA expression							
Low	233 (53)				1 (Reference)		1 (Reference)
High	260 (47)	0.002	0.007	0.012	1.80 (1.14, 2.84)	0.011	2.15 (1.20, 3.86)

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; CT, chemotherapy.

Supplementary Table S5

Association between *SLC7A5* mRNA expression and clinicopathological characteristics in ERα-positive breast cancer patients

	All patients	*SLC7A5* mRNA expression		
		Low	High	*P* value
	n (%)	n (%)	n (%)	
Patients	491	175	316	
Menopausal status				0.058
Pre	216 (44)	87 (50)	129 (41)	
Post	275 (56)	88 (50)	187 (59)	
Tumor size				1
≤2cm	207 (42)	74 (42)	133 (42)	
>2cm	284 (58)	101 (58)	183 (58)	
Nodal status				0.009
Negative	258 (53)	106 (61)	152 (48)	
Positive	209 (43)	61 (35)	148 (47)	
Unknown	24 (5)	8 (4)	16 (5)	
Grade				0.008
1	160 (33)	65 (37)	95 (30)	
2	155 (32)	63 (36)	92 (29)	
3	144 (29)	43 (25)	121 (38)	
Unknown	12 (2)	4 (2)	8 (3)	
Histology				0.46
IDC	438 (89)	152 (87)	286 (91)	
ILC	26 (5)	10 (6)	16 (5)	
Others	27 (6)	12 (7)	14 (4)	
PgR status				1
Positive	426 (87)	152 (87)	274 (87)	
Negative	65 (13)	23 (13)	42 (13)	
HER2 status				1
Positive	45 (9)	17 (10)	28 (10)	
Negative	429 (87)	153 (87)	276 (87)	
Unknown	17 (4)	5 (3)	12 (3)	
Adjuvant therapy				
ET alone	251 (51)	103 (58)	148 (47)	
CT alone	29 (6)	4 (2)	25 (8)	
ET+CT	173 (35)	57 (33)	116 (37)	
None	31 (7)	10 (6)	21 (6)	
Unknown	7 (1)	1 (1)	6 (2)	
Endocrine therapy				
With tamoxifen	272 (56)	105 (60)	167 (53)	
Without tamoxifen	181 (31)	59 (34)	122 (37)	
None	31 (12)	10 (6)	21 (7)	
Unknown	7 (1)	1 (0)	6 (2)	

PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; CT, chemotherapy.

Supplementary Table S6

Association between *LLGL2* and *SLC7A5* mRNA co-expression and clinicopathological characteristics in all breast cancer patients

	LLGL2/SLC7A5				
	Low/Low n (%)	High/Low n (%)	Low/High n (%)	High/High n (%)	*P* value
Patients	91	101	246	186	
Menopausal status					
Pre	49 (39)	48 (48)	97 (40)	68 (37)	0.026
Post	42 (61)	53 (52)	147 (60)	118 (63)	
Tumor size					
≤2cm	31 (34)	47 (46)	86 (35)	76 (41)	0.162
>2cm	60 (66)	54 (54)	159 (65)	110 (59)	
Unknown			1 (0.4)		
Nodal status					
Negative	62 (68)	56 (55)	134 (54)	87 (47)	0.007
Positive	25 (28)	41 (41)	100 (41)	91 (49)	
Unknown	4 (4)	4 (4)	12 (5)	8 (4)	
pStage TNM[*1]					
I	30 (33)	32 (32)	62 (25)	47 (25)	0.047
II	46 (51)	48 (47)	119 (48)	91 (49)	
III	11 (12)	15 (15)	51 (21)	38 (21)	
Unknown	4 (4)	6 (6)	14 (6)	10 (5)	
Grade					
1+2	66 (73)	64 (63)	121 (49)	104 (56)	0.0008
3	23 (25)	35 (35)	118 (48)	77 (41)	
Unknown	2 (2)	2 (2)	7 (3)	5 (3)	
Histology					
IDC	78 (87)	89 (88)	223 (91)	166 (89)	0.23
ILC	4 (4)	6 (6)	5 (2)	12 (7)	
Others	8 (9)	6 (6)	18 (7)	8 (4)	
Unknown			1 (0.4)		
ERα status					
Positive	84 (92)	91 (90)	175 (71)	141 (76)	<0.001
Negative	7 (8)	10 (10)	70 (29)	45 (24)	
Unknown			1 (0.4)		
PgR status					
Positive	77 (85)	79 (78)	162 (66)	124 (67)	0.002
Negative	14 (15)	22 (22)	83 (34)	62 (33)	
Unknown			1 (0.4)		
HER2 status					
Positive	7 (8)	16 (16)	33 (13)	26 (14)	0.59
Negative	79 (87)	83 (82)	204 (83)	152 (82)	
Unknown	5 (5)	2 (2)	9 (4)	8 (4)	
Adjuvant therapy					
ET alone	58 (64)	48 (47)	92 (37)	67 (36)	
CT alone	6 (7)	5 (5)	56 (23)	25 (13)	
ET+CT	24 (26)	38 (37)	68 (28)	76 (41)	
None	3 (3)	9 (9)	23 (9)	16 (9)	
Unknown		1 (1)	7 (3)	2 (1)	

ERα, estrogen receptor α; PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma;

HER2, human epidermal growth factor receptor 2; ET, endocrine therapy; CT, chemotherapy.

*1: AJCC stage

Supplementary Table S7

Univariate and multivariate analyses of factors associated with DFS and OS including *LLGL2*/*SLC7A5* in all patients

Variate	n (%)	Univariate (DFS) P-value	Univariate (OS) P-value	Multivariate (DFS) P-value	HR (95% CI)	Multivariate (OS) P-value	HR (95% CI)
Age							
≤ 50	236 (42)						
> 50	324 (58)	0.34	0.53				
Menopausal status							
Pre	247 (44)						
Post	313 (56)	0.49	0.44				
Tumor size							
≤ 2 cm	215 (38)						1 (Reference)
> 2 cm	345 (62)	0.041	0.003			0.06	1.53 (0.98, 2.39)
Nodal status							
Negative	316 (56)				1 (Reference)		1 (Reference)
Positive	244 (44)	< 0.0001	< 0.0001	< 0.0001	3.49 (2.48, 4.92)	< 0.0001	3.42 (2.26, 5.18)
Grade							
1 and 2	323 (58)						
3	237 (42)	0.039	0.022				
Histology							
IDC	509 (91)						
ILC	19 (3)	0.93	0.67				
Others	32 (6)	0.20	0.47				
ERα status							
Positive	443 (79)				1 (Reference)		1 (Reference)
Negative	117 (21)	0.001	0.001	0.0003	1.94 (1.36, 2.78)	0.001	1.99 (1.31, 3.01)
HER2 status							
Negative	484 (86)						
Positive	76 (14)	0.042	0.042				
LLGL2/SLC7A5							
Low/Low	81 (14)				1 (Reference)		1 (Reference)
High/Low	94 (17)	0.004	0.032	0.013	2.95 (1.26, 6.92)	0.051	3.12 (0.99, 9.75)
Low/High	218 (39)	0.0005	0.001	0.007	2.98 (1.35, 6.54)	0.008	3.98 (1.42, 11.13)
High/High	167 (30)	< 0.0001	0.0003	0.002	3.49 (1.58, 7.72)	0.003	4.79 (1.70, 13.52)

ERα, estrogen receptor α; PgR, progesterone receptor; IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; HER2, human epidermal growth factor receptor 2.