

SLC1A5 co-expression with TALDO1 associates with endocrine therapy failure in oestrogen receptor-positive breast cancer

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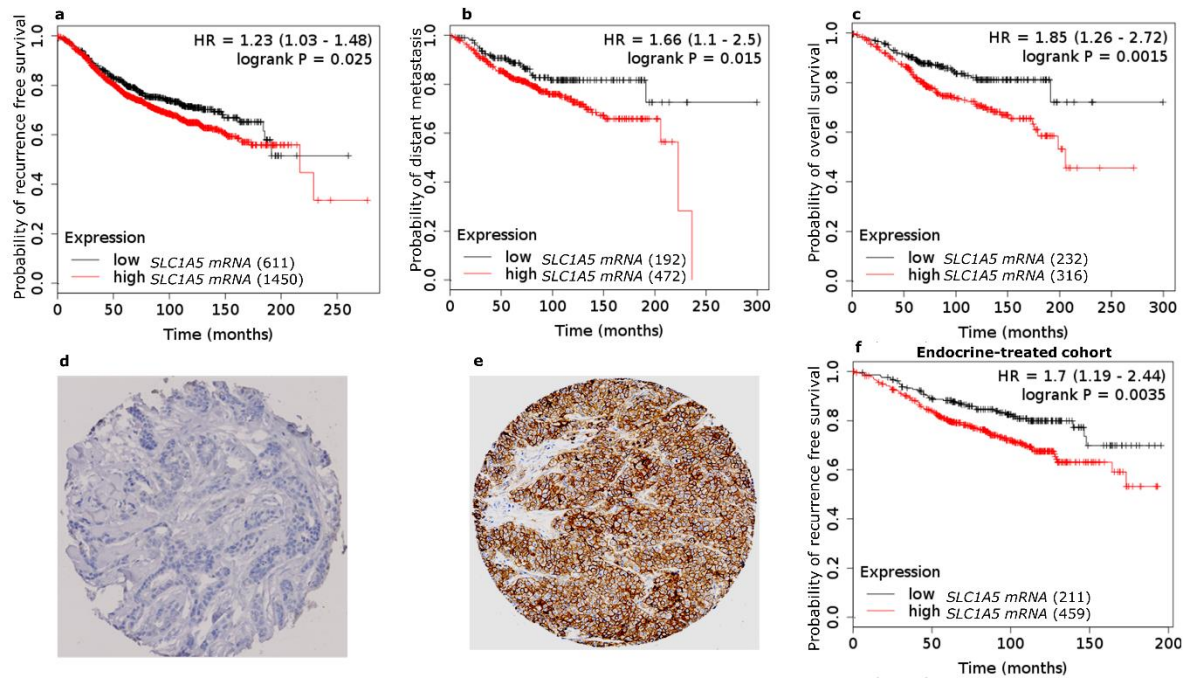
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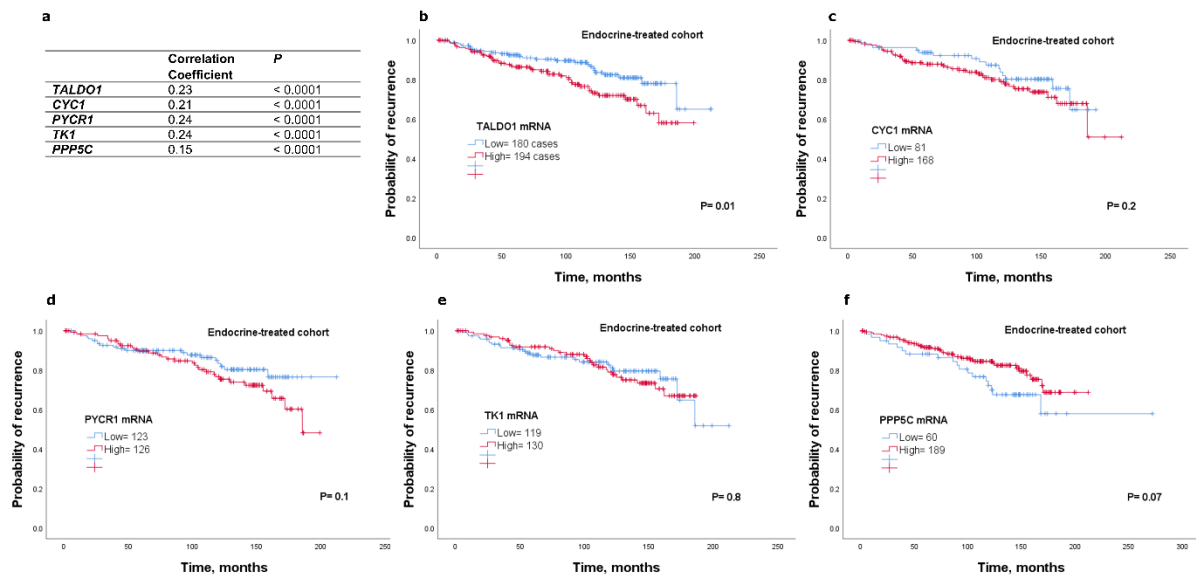
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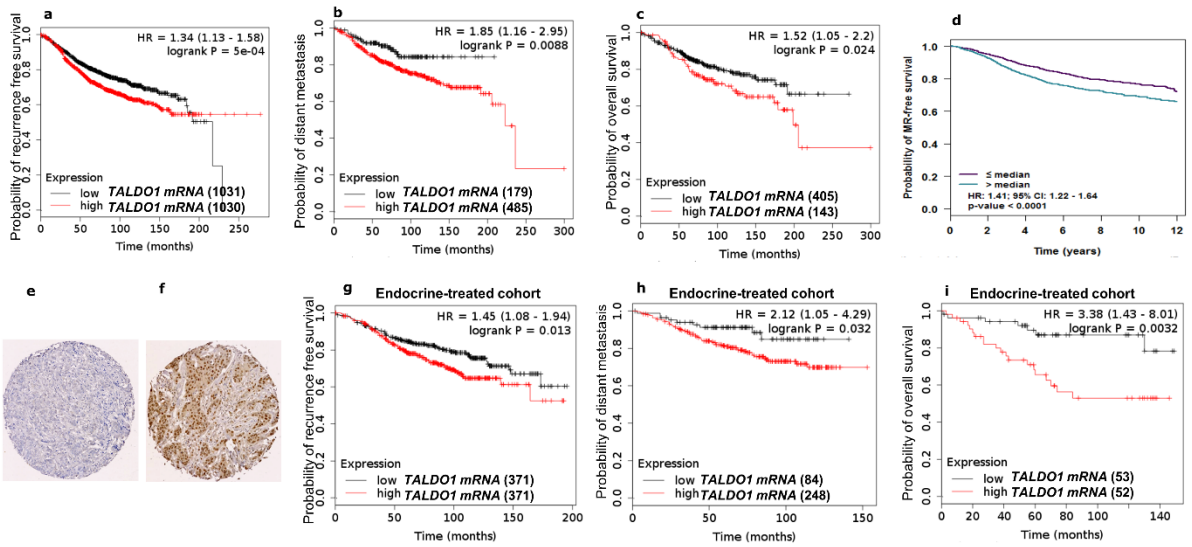
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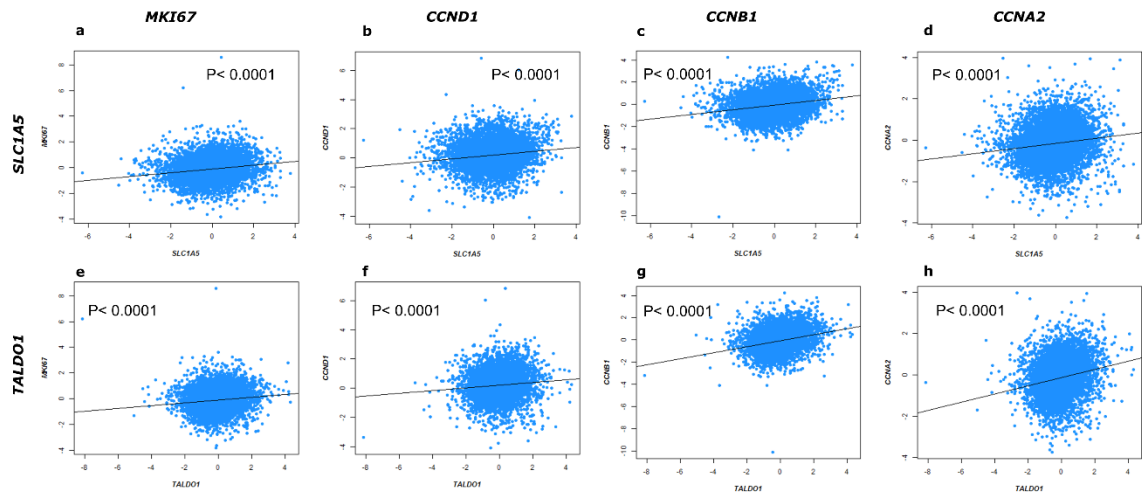
Supplementary figure 1: Kaplan–Meier of *SLC1A5* mRNA and patient outcome in luminal breast cancer using KM-Plotter for **a)** recurrence free survival **b)** distant metastasis and **c)** overall survival. Representative immunostaining images of invasive breast cancer cores using IHC **d)** Negative and **e)** positive for *SLC1A5* protein expression. Kaplan-Meier of *SLC1A5* mRNA expression in patients with luminal breast cancer who received endocrine treatment only using KM-Plotter dataset **f)** recurrence free survival.



Supplementary figure 2: a) shows correlation of *TALDO1*, *CYC1*, *PYCR1*, *TK1* and *PPP5C* with *SLC1A5* mRNA expression using bc-GenExMiner v4.3. Kaplan-Meier analysis and recurrence in patients with luminal breast cancer who received endocrine treatment only using METABRIC cohort for **b) TALDO1** **c) CYC1** **d) PYCR1** **e) TK1** and **f) PPP5C**.



Supplementary figure 3: Kaplan–Meier of *TALDO1* mRNA and patient outcome in luminal breast cancer using KM-Plotter dataset for **a**) recurrence free survival **b**) distant metastasis and **c**) overall survival, while **d**) Kaplan–Meier using bc-GenExMiner v4.3 for *TALDO1* mRNA and survival. Representative immunostaining images of invasive breast cancer cores using IHC **e**) Negative and **f**) Positive for *TALDO1* protein expression. Kaplan–Meier of *TALDO1* mRNA expression in patients with luminal breast cancer who received endocrine treatment only using KM-Plotter **g**) recurrence free survival **h**) distant metastasis and **i**) overall survival.



Supplementary figure 4: *SLC1A5* mRNA correlation with proliferation associated-genes including **a) MKI67** **b) CCND1** **c) CCNB1** and **d) CCNA2**, and *TALDO1* mRNA correlation with **e) MKI67** **f) CCND1** **g) CCNB1** and **h) CCNA2** using bc-GenExMiner v4.3 dataset.

Supplementary table 1: Clinicopathological characteristics of luminal breast cancer cohorts.

Parameters	METABRIC cohort	Nottingham cohort
	<i>mRNA</i>	Protein
	No. (%)	No. (%)
Age		
<50	228 (15)	449 (31)
≥50	1278 (85)	1006 (69)
Tumour size (cm)		
<2 cm	475 (31.5)	806 (55.7)
≥2 cm	1031 (68.5)	640 (44.3)
Tumour grade		
1	166 (11.5)	388 (24.7)
2	707 (49.1)	661 (42.1)
3	565 (38.4)	522 (33.2)
Nottingham Prognostic Index		
GPG	623 (41.3)	598 (41.4)
MPG	772 (51.2)	668 (46.1)
PPG	111 (7.5)	180 (12.5)
Nodal stage		
1	404 (36.2)	1025 (65.1)
2	634 (56.8)	439 (27.9)
3	78 (7)	111 (7)
Vascular invasion		
negative	N/A	1000 (69)
positive		439 (31)
Endocrine therapy alone		
No	234 (15.5)	810 (50)
Yes	384 (25.5)	554 (35)
Other*	888 (59)	237 (15)
Recurrence		
No	496 (33)	953 (60)
Yes	118 (7)	618 (38)
Unknown	892 (60)	30 (2)
Distant metastasis		
No	476 (31)	1079 (67)
Yes	143 (10)	514 (32)
Unknown	887 (59)	8 (1)
Progesterone receptor		
Negative	486 (23.2)	300 (21.3)
Positive	1020 (76.8)	1103 (78.7)

GPG: Good prognostic group; **MPG:** Moderate prognostic group; **PPG:** Poor prognostic group

***:** Include patients who received chemotherapy alone or combination of chemotherapy and endocrine therapy.

Supplementary table 2: Multivariate cox analysis of associations between SLC1A5 protein expression and clinicopathological parameters using Nottingham cohort.

Luminal breast cancer cohort			
	Distant metastasis free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5	1.2 (1.0-1.5)	0.028	0.03
Tumor size	1.5 (1.2-1.8)	0.00005	0.0001
Tumor grade	1.5 (1.3-1.8)	1.7e-10	< 0.0001
Nodal stage	1.8 (1.5-2.1)	7.9e-17	< 0.0001
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5	1.3 (1.0-1.6)	0.01	0.012
Tumor size	1.4 (1.1-1.8)	0.0003	0.0005
Tumor grade	1.6 (1.4-1.9)	2.2e-11	< 0.0001
Nodal stage	1.6 (1.4-1.8)	1.7e-10	< 0.0001
Endocrine-treated cohort			
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5	1.4 (1.0-1.9)	0.029	0.03
Tumor size	1.4 (1.0-2.0)	0.026	0.04
Tumor grade	2.2 (1.6-3.1)	1.5e-7	< 0.0001
Nodal stage	1.9 (1.5-2.4)	1.3e-7	< 0.0001

*P**: Adjusted p-value

Supplementary table 3: Multivariate cox analysis of associations between TALDO1 protein expression and clinicopathological parameters using Nottingham cohort.

Luminal breast cancer cohort			
	Recurrence free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	1.5 (1.1-2.1)	0.006	0.01
Tumor size	1.5 (1.0-2.1)	0.013	0.02
Tumor grade	1.2 (1.0-1.6)	0.033	0.04
Nodal stage	1.5 (1.2-1.9)	0.0002	0.001
	Distant metastasis free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	1.5 (1.1-2.1)	0.009	0.01
Tumor size	2.0 (1.4-2.9)	0.00003	0.0002
Tumor grade	1.3 (1.0-1.7)	0.01	0.012
Nodal stage	1.5 (1.2-2.0)	0.0001	0.0003
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	1.8 (1.2-2.5)	0.001	0.0013
Tumor size	2.0 (1.3-3.0)	0.00042	0.001
Tumor grade	1.6 (1.2-2.2)	0.00046	0.008
Nodal stage	1.7 (1.3-2.3)	0.00001	0.0001
Endocrine-treated cohort			
	Recurrence free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	2.2 (1.3-3.6)	0.001	0.002
Tumor size	1.6 (1.0-2.7)	0.03	0.05
Tumor grade	1.5 (0.9-2.2)	0.05	0.06
Nodal stage	1.7 (1.2-2.3)	0.001	0.005
	Distant metastasis free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	2.3 (1.4-3.9)	0.001	0.002
Tumor size	1.9 (1.1-3.3)	0.01	0.015
Tumor grade	1.7 (1.1-2.7)	0.012	0.016
Nodal stage	1.7 (1.2-2.3)	0.001	0.005
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
TALDO1	2.4 (1.4-4.1)	0.001	0.002
Tumor size	2.0 (1.1-3.5)	0.013	0.016
Tumor grade	2.2 (1.3-3.6)	0.001	0.002
Nodal stage	1.7 (1.2-2.4)	0.002	0.005
<i>P*</i> : Adjusted p-value			

Supplementary table 4: Multivariate cox analysis of associations between SLC1A5/TALDO1 protein co-expression and clinicopathological parameters using Nottingham cohort.

Luminal breast cancer cohort			
	Recurrence free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	1.5 (1.0-2.4)	0.03	0.05
Tumor size	1.5 (1.1-2.1)	0.008	0.02
Tumor grade	1.2 (1.0-1.6)	0.04	0.05
Nodal stage	1.5 (1.1-1.9)	0.001	0.005
	Distant metastasis free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	1.7 (1.0-2.7)	0.02	0.025
Tumor size	2.1 (1.5-3.1)	0.00002	0.0001
Tumor grade	1.3 (1.0-1.7)	0.01	0.016
Nodal stage	1.5 (1.2-1.9)	0.0003	0.0008
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	2.1 (1.2-3.6)	0.005	0.006
Tumor size	2.0 (1.3-3.0)	0.0004	0.001
Tumor grade	1.6 (1.2-2.2)	0.002	0.003
Nodal stage	1.7 (1.3-2.2)	0.00004	0.0002
Endocrine-treated cohort			
	Recurrence free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	2.5 (1.3-4.7)	0.005	0.01
Tumor size	1.6 (1.0-2.7)	0.04	0.06
Tumor grade	1.4 (0.9-2.1)	0.1	0.12
Nodal stage	1.6 (1.1-2.3)	0.003	0.01
	Distant metastasis free survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	2.5 (1.3-4.9)	0.006	0.01
Tumor size	1.9 (1.1-3.2)	0.01	0.016
Tumor grade	1.6 (1.0-2.6)	0.03	0.037
Nodal stage	1.6 (1.1-2.3)	0.004	0.02
	Breast cancer specific survival		
	HR (95% CI)	<i>P</i>	<i>P*</i>
SLC1A5+TALDO1+ vs SLC1A5-TALDO1-	2.6 (1.3-5.4)	0.007	0.01
Tumor size	1.9 (1.1-3.3)	0.02	0.025
Tumor grade	2.0 (1.2-3.4)	0.005	0.01
Nodal stage	1.6 (1.1-2.4)	0.005	0.02

*P**: Adjusted p-value

Supplementary table 5: Correlation of *SLC1A5* and *TALDO1* mRNA expression with the proliferation related-genes in luminal breast cancer using METABRIC cohort.

	<i>SLC1A5</i> mRNA		
	Correlation Coefficient	<i>P</i>	<i>P</i> *
<i>MKI67</i>	0.21	7.89e-18	< 0.0001
<i>CCNB1</i>	0.25	6.21e-24	< 0.0001
<i>CCNA2</i>	0.19	1.01e-13	< 0.0001
<i>CCND1</i>	0.17	6.80e-12	< 0.0001
	<i>TALDO1</i> mRNA		
	Correlation Coefficient	<i>P</i>	<i>P</i> *
<i>MKI67</i>	0.12	5.93e-7	< 0.0001
<i>CCNB1</i>	0.08	0.002	0.0027
<i>CCNA2</i>	0.33	1.91e-40	< 0.0001
<i>CCND1</i>	-0.004	0.89	3.56
<i>P</i>* : Adjusted p-value			