RESEARCH

TRPS1, a sensitive marker for different histological and molecular types of breast cancer

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Abstract

Objectives We explored Trichorhinophalangeal syndrome type 1 (TRPS1) expression in special types of breast carcinoma, and analyzed the correlation between TRPS1 and androgen receptor (AR) expression in triple-negative breast cancer (TNBC).

Methods TRPS1 expression was analyzed in 801 patients with special types of breast carcinoma. A total of 969 TNBC were used to analyze the correlation between the expression of TRPS1 and AR. TRPS1 expression was evaluated in 1975 cases of breast cancer with different molecular types.

Results A total of 801 special types of breast cancers were stained with TRPS1. TRPS1 was positive in 100% (63/63) of mucinous carcinoma, 100% (7/7) adenoid cystic carcinomas (4 classic adenoid cystic carcinomas and 3 solid-basaloid adenoid cystic carcinomas), 100% (4/4) tubular carcinomas, 100% (2/2) secretory carcinomas, and 99.59% (243/244) invasive lobular carcinomas, 99.26% (267/269) invasive micropapillary carcinomas, 97.44% (38/39) ER-positive neuroendocrine tumors, 94.44% (34/36) metaplastic breast carcinomas (MBCs), 63.73% (65/102) apocrine carcinomas. TRPS1 was negative in all triple-negative neuroendocrine carcinomas (0/7). TRPS1 was positive in 92.86% (26/28) of metastatic special types of breast cancer. TRPS1 and AR expression were analyzed in 969 cases of TNBC. 90.40% were positive for TRPS1, and 42.41% were positive for AR. A significant inverse correlation between TRPS1 and AR expression was shown in TNBC ($p < .001$). TRPS1 showed a higher positive rate (93.13%) in TNBC compared to GATA binding protein 3 (GATA3), gross cystic disease fluid protein 15 (GCDFP-15) and forkhead box transcription Factor C 1 (FOXC1).

Conclusions In conclusion, our study demonstrated that TRPS1 is a highly sensitive marker for most special types of breast carcinoma. TRPS1 was positive in 63.73% of apocrine carcinomas. TRPS1 and AR expression was inversely correlated in TNBC.

Keywords Special types of breast carcinoma, Immunohistochemistry, TRPS1, GATA3, AR, GCDFP-15, FOXC1

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Introduction

Considering the high incidence and high rate of metastasis of breast cancer, metastatic breast carcinoma is commonly considered when metastatic disease is detected in lymph nodes or organs such as the lung, liver, bone, and brain in females. Immunohistochemical analysis is the most common way to identify breast cancer origin in addition to clinical history and histological features. GATA binding protein 3 (GATA3), gross cystic disease fluid protein 15 (GCDFP-15) and forkhead box transcription Factor C 1 (FOXC1) are relatively sensitive markers for breast cancer. GATA3 and GCDFP-15 are luminal markers, and the overall sensitivities of GATA3 and GCDFP-15 to breast cancer are approximately 70%-90% and 25–60%, respectively [1–3]. However, the expression of GATA3 and GCDFP-15 is low in triple-negative breast cancer (TNBC) [4–6]. Moreover, GATA3 and GCDFP-15 are expressed in urothelial carcinoma, salivary ductal carcinoma, skin adnexal tumors, T-cell lymphoma, prostate carcinoma and sweat gland carcinoma [3, 7, 8]. FOXC1 is a reliable marker of TNBC and little expressed in luminal and human epidermal growth factor receptor 2 (HER2)-positive invasive breast carcinomas (IBCs) [9]. Thus, there is a need to identify novel sensitive and specific markers to determine breast origin.

Trichorhinophalangeal syndrome type 1 (TRPS1) is a newly discovered marker in the GATA family of zinc finger transcription factors. According to previous studies, TRPS1 is significantly upregulated in breast carcinomas compared with normal breast cells [10]. TRPS1 functions as an essential regulator of the growth and differentiation of normal mammary epithelial cells and may be involved in the development of breast cancer. Recent studies have revealed that TRPS1 is a specific and sensitive marker for breast cancer [11–13]. TRPS1 is highly expressed in 4 molecular types of breast cancer, especially TNBCs [14]. Moreover, TRPS1 showed no or little expression in some tumor types, including lung adenocarcinoma, pancreatic adenocarcinoma, colon and gastric adenocarcinoma, renal cell carcinoma and melanoma [14].

TRPS1 has been analyzed in some specific types of breast cancer, such as invasive lobular carcinoma, metaplastic breast carcinoma (MBC), neuroendocrine carcinomas, acinic cell carcinomas, cribriform adenoid cystic carcinomas (AdCCs) and secretory carcinoma (SC) [15]. However, the sample sizes of these studies were relatively small. Some studies have revealed that TRPS1 is expressed in androgen receptor (AR)-positive apocrine carcinoma, but the results are conflicting. In addition, the correlation between TRPS1 and AR expression in TNBC has not been well studied. Some studies have reported TRPS1 expression in metastatic IBC. Wang et al. [16] reported that TRPS1 had a high sensitivity of 88% for metastatic TNBC. However, research on TRPS1 expression in the most clinically challenging context of identifying a special metastatic type of breast cancer (BC) is limited. Previous studies have frequently compared TRPS1 with GATA3 expression in breast cancers [4]; however, few studies have compared the expression of TRPS1 and FOXC1, especially in TNBC.

The main objective of the current study was to explore TRPS1 expression in special types of breast carcinoma (primary and metastatic). The secondary aims of the study included to assess the correlation between TRPS1 and AR expression in TNBC, and the expression of TRPS1, GATA3, GCDFP-15 and FOXC1 in the immunohistochemistry (IHC)—based molecular types of IBC. To the best of our knowledge, this is the largest reported series of TRPS1 expression in China.

Materials and methods

Study design and case selection

Our study was divided into three parts: (1) evaluating TRPS1 in 801 patients with special types of BC; (2) analysing the correlation between TRPS1 and AR in 969 patients with TNBC (most of them were IBC of no special type); and (3) comparing the expression of TRPS1, GATA3, GCDFP-15 and FOXC1 in 1975 patients with different molecular types of BC (most of them were luminal breast cancers). All samples were collected from 2021–2023 in Fudan University Shanghai Cancer Center.. Tissue samples were obtained from surgical resection. The IHC was performed on full sections. All the pathological sections were reviewed, and the histological diagnosis was made according to the 5th edition of the World Health Organization (WHO) classification. All special types of breast carcinoma were composed of > 90% special carcinoma components according to WHO classification.

Immunohistochemistry

The details of the IHC antibodies used are shown in Table 1. All staining was performed with a Ventana BenchMark Ultra autostainer (Ventana Medical System Inc., Roche, Tucson, Arizona). According to the Bench-Mark ULTRA advanced staining system operator guide, the staining process was performed by applying the appropriate reagent, monitoring the incubation time, and rinsing slides between reagents. Only nuclear staining was considered to indicate positive TRPS1, GATA3, FOXC1 and AR expression, whereas cytoplasmic staining indicated positive GCDFP-15 expression. The expression of these proteins was divided by the percentage of positive cells (negative, < 1%; low positive, 1–10%; intermediate positive, 11–50%; high positive, 51–100%). Patients with intermediate to high positive expression were

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Table 1 Antibodies Used for Immunohistochemistry

Antibody	Clone	Dilution	Source
TRPS1	EPR16171	1:8000	Abcam
GATA3	L50-823	Predilute	Roche
GCDFP-15	23A3	Predilute	Leica Biosystems
FOXC1	EPR20685	1:500	Abcam
ER	SP1	Predilute	Ventana Medical Systems, Inc
PR	IE2	Predilute	Ventana Medical Systems, Inc
HER2	4B5	Predilute	Ventana Medical Systems, Inc
Ki-67	30–9	Predilute	Ventana Medical Systems, Inc
AR	EPR1535	1:200	Abcam

regarded as positive cases, and those with low positive expression were grouped as negative expression.

The immunohistochemical surrogate type of all included IBCs was determined using the following definitions according to the 2013 St Gallen Consensus: luminal A subtype (estrogen receptor (ER)+, progesterone receptor (PR)+ ≥ 20%), HER2-, and Ki-67 < 20%), luminal B subtype (ER+, HER2-, Ki-67 > 20% or PR-/+; ER+, HER2+with any PR or Ki-67 index), HER2+subtype (ER-,PR-,HER2+) and triple-negative subtype (ER-, PR- and HER2-). According to the 2020 American Society of Clinical Oncology/College of American Pathologists (ASCO/CAP) guidelines [17], nuclear ER/PR staining in 1% or more of samples was defined as ER/PR-positive. HER2 status was assessed as proposed in the 2023 ASCO/CAP guidelines [18]. HER2 was considered positive if the patient had an IHC score of 3+ or HER2 gene amplification. Ki-67 interpretation standards referred to the 2011 recommendations from the International Ki-67 in Breast Cancer Working Group [19]. Ki-67 values less than 20% were considered low; otherwise, they were considered high.

Statistical analysis

SPSS software version 19 was used to perform all the statistical analyses. The data were compared between different subgroups, and the correlation between the expression of AR and that of TRPS1 was analyzed by using χ^2 analysis or Fisher's exact test. The level of significance was set at 0.05. A *p* value < 0.05 was considered to indicate statistical significance.

Results

Expression of TRPS1 in special types of breast carcinoma

A total of 801 special types of breast cancers were stained with TRPS1 and GATA3. TRPS1 and GATA3 were positive in 100% (63/63) and 100% (63/63) of mucinous carcinoma, 100% (7/7) and 0% (0/3) adenoid cystic carcinomas

(4 classic adenoid cystic carcinomas and 3 solid-basaloid adenoid cystic carcinomas), 100% (4/4) and 100% (4/4) tubular carcinomas, 100% (2/2) and 100% (2/2) secretory carcinomas, 99.59% (243/244) and 100% (244/244) invasive lobular carcinomas, 99.26% (267/269) and 98.51% (265/269) invasive micropapillary carcinomas, 97.44% (38/39) and 100% (34/34) ER-positive neuroendocrine tumors. TRPS1 and GATA3 were negative in all triple-negative neuroendocrine carcinomas (0/7). The above data are shown in Table 2 and Fig. 1.

Among all subtypes of MBC, 94.44% (34/36) were positive for TRPS1, and 41.18% (14/34) were positive for GATA3 (Table 3). Among the 13 squamous cell carcinomas, 84.62% (11/13) were positive for TRPS1, and 46.15% (6/13) were positive for GATA3. In 1 patient with fibromatosis-like MBC, TRPS1 was weakly positive. Among the metaplastic carcinoma with mesenchymal differentiation (MC-MD), 100% (22/22) were positive for TRPS1, whereas 38.10% (8/21) were positive for GATA3.

TRPS1 and GATA3 expression was also analyzed by IHC in 102 patients with apocrine carcinomas (AR positive and ER-negative), including 77 patients with a triple-negative phenotype and 25 patients with a HER2-positive phenotype (Table 4 and Fig. 2). Among the apocrine carcinomas, 63.73% (65/102) were positive for TRPS1, and 86.27% (88/102) were positive for GATA3. TRPS1 expression was positive in 58.44% (45/77) of the triple-negative phenotype and 80% (20/25) of the HER2-positive phenotype. GATA3 was positive in 84.42% (65/77) of the triple-negative phenotype and 92% (23/25) of the HER2-positive phenotype.

A total of 28 patients had metastatic special types of BC, including 14 cases of invasive lobular carcinoma, 7 cases of neuroendocrine tumors of the breast (including 6 ER-positive neuroendocrine tumors and 1 triple-negative neuroendocrine carcinoma), 6 cases of MC-MD, and 1 case of invasive micropapillary carcinoma. These tumors generally metastasize to organs such as the lung, liver, bone, and brain (Table 5). TRPS1 and GATA3 were positive in 100% (1/1) and 100% (1/1) of invasive micropapillary carcinomas, 100% (6/6) and 100% (6/6) ER-positive neuroendocrine tumors of the breast, 100% (6/6) and 20% (1/5) MC-MD, 92.86% (13/14) and 100% (11/11) invasive lobular carcinomas. TRPS1 and GATA3 were negative in 1 patient with triple-negative neuroendocrine carcinoma of the breast. The above data are shown in Table 6.

Correlation of TRPS1 and AR expression in TNBC

TRPS1 and AR expression was analyzed by IHC in 969 patients diagnosed with TNBC (Table 7). We found that 90.40% were positive for TRPS1, and 42.41% were positive for AR. A significant inverse correlation between

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Table 2 Expression of TRPS1 and GATA3 in special types of BCs

Histologic type	Molecular subtype	TRPS1					GATA3				
		Negative	Low	moderate	High	Total positive (%)	Negative	Low	moderate	High	Total positive (%)
invasive micropapillary carcinoma	Luminal/HER2 + /triple negative	1	1	1	266	99.26% (267/269)	0	4	4	261	98.51% (265/269)
invasive lobular carcinoma	Luminal/HER2 + /triple negative	0	1	0	243	99.59% (243/244)	0	0	0	244	100% (244/244)
mucinous carcinoma	luminal	0	0	0	63	100% (63/63)	0	0	0	63	100% (63/63)
ER-positive neuroendocrine tumor	luminal	0	1	0	38	97.44% (38/39)	0	0	0	34	100% (34/34)
triple-negative neuroendocrine carcinoma	triple negative	5	2	0	0	0% (0/7)	6	0	0	0	0% (0/6)
adenoid cystic carcinoma	triple negative	0	0	2	5	100% (7/7)	3	0	0	0	0% (0/3)
tubular carcinoma	luminal	0	0	0	4	100% (4/4)	0	0	0	4	100% (4/4)
secretory carcinoma	triple negative	0	0	0	2	100% (2/2)	0	0	0	2	100% (2/2)

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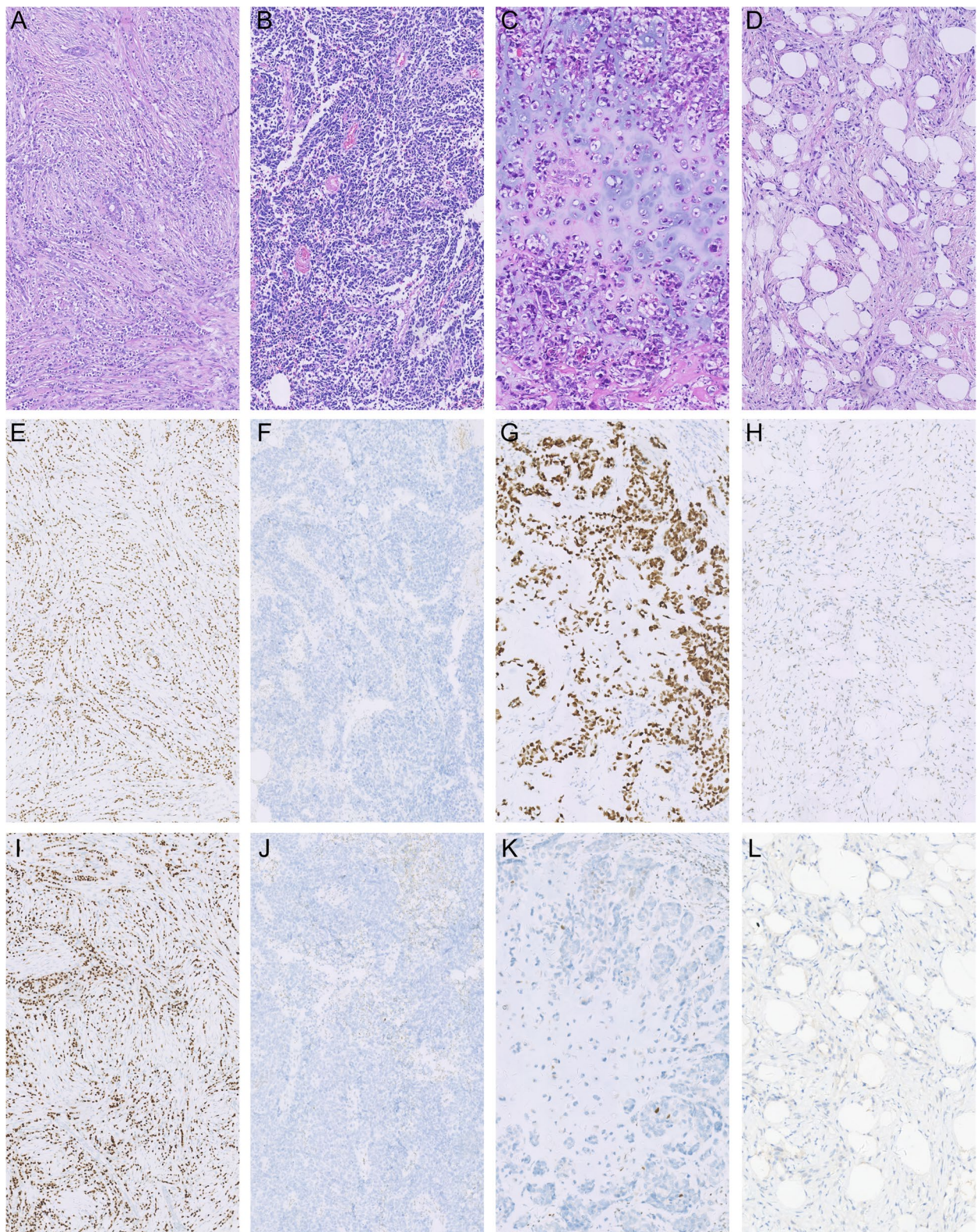
Fig. 1 Morphological and immunohistochemical staining patterns of TRPS1 and GATA3 for representative examples of special types of breast cancer with various staining patterns for these markers (20×). **A**, **E**, **I** Invasive lobular carcinoma. **B**, **F**, **J** triple-negative neuroendocrine carcinoma. **C**, **G**, **K** MC-MD. **D**, **H**, **L** Fibromatosis-like MBC. A–D: HE; E–H: TRPS1; I–L: GATA3

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Table 3 Expression of TRPS1 and GATA3 in MBCs

Histologic type	Molecular subtype	TRPS1					GATA3				
		Negative	Low	moderate	High	Total positive (%)	Negative	Low	moderate	High	Total positive (%)
squamous cell carcinomas	triple negative	0	2	1	10	84.62%(11/13)	0	7	3	3	46.15% (6/13)
fibromatosis-like MBC	triple negative	0	0	0	1	100%(1/1)	0	0	0	0	0
MC-MD	triple negative	0	0	1	21	100% (22/22)	9	4	4	4	38.10% (8/21)

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Table 4 Expression of TRPS1 and GATA3 in apocrine carcinomas

Histologic type	Molecular subtype	TRPS1					GATA3				
		Negative	Low	moderate	High	Total positive (%)	Negative	Low	moderate	High	Total positive (%)
apocrine carcinoma	HER2 +	2	3	1	19	80%(20/25)	1	1	0	23	92%(23/25)
apocrine carcinoma	triple negative	14	18	17	28	58.44%(45/77)	0	12	11	54	84.42%(65/77)
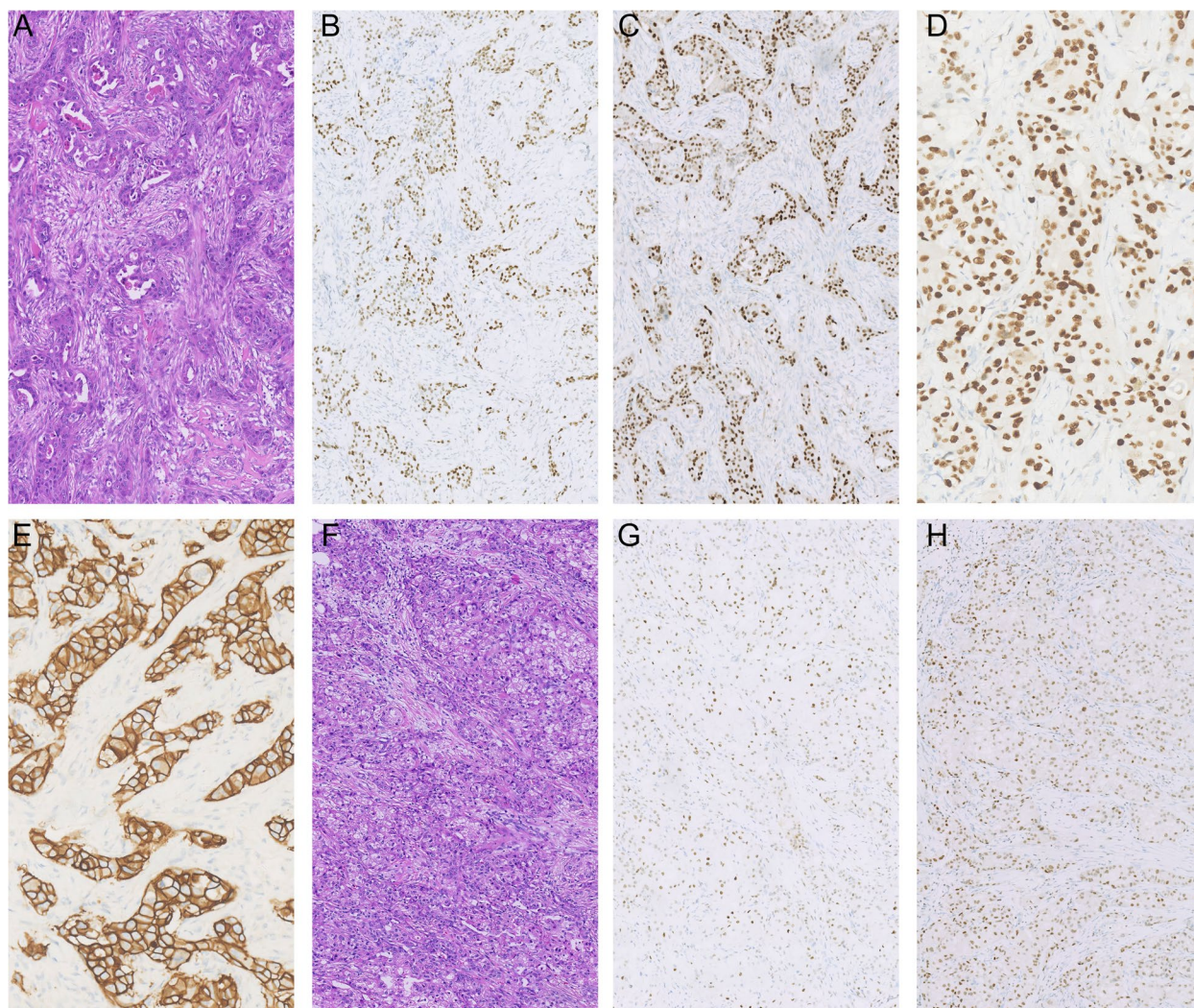
Fig. 2 TRPS1 and GATA3 expression in apocrine carcinoma (20×). **A-E** HER2 positive apocrine carcinoma. H&E staining (**A**), TRPS1 high positive expression (**B**), GATA3 high positive expression (**C**), AR expression (**D**) and HER2 expression (**E**). F–H: Triple-negative apocrine carcinoma. H&E staining (**F**) and TRPS1 low positive expression (**G**) and GATA3 high positive expression (**H**)

Table 5 Metastatic sites of metastatic special types of BC

Histologic type	metastatic sites	Total
invasive lobular carcinoma	brain, liver, bone	14
ER-positive neuroendocrine tumor	bone	6
triple-negative neuroendocrine carcinoma	liver	1
MC-MD	lung	6
invasive micropapillary carcinoma	liver	1

TRPS1 and AR expression was shown in TNBC ($p < 0.001$). A total of 538 patients (55.52%) were TRPS1 positive and AR negative, and 73 patients (7.53%) were AR positive and TRPS1 negative.

Expression of TRPS1, GATA3, GCDFP-15 and FOXC1 in 4 molecular types of breast cancer

Four markers (TRPS1, GATA3, GCDFP-15, and FOXC1) were analyzed in a total of 1975 patients with breast cancer, including 607 patients with luminal A breast cancer, 708 patients with luminal B breast cancer, 296 patients with HER2 + breast cancer and 364 patients with triple-negative breast cancer. Our results revealed no difference in the percentage of luminal A breast cancers positive for TRPS1 or GATA3 (99.84% vs. 99.84%, respectively) and luminal B breast cancer (99.15% vs. 99.58%). However, differences in the expression of TRPS1 and GATA3 were most prominent in TNBC (93.13% vs. 53.57%), followed by HER2 + breast cancer (98.99% vs. 87.16%). We also tested GCDFP-15

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Table 6 Expression of TRPS1 and GATA3 in metastatic special types of BC

Histologic type	Molecular subtype	TRPS1					GATA3				
		Negative	Low	moderate	High	Total positive (%)	Negative	Low	moderate	High	Total positive (%)
invasive lobular carcinoma	Luminal/triple negative	1	0	0	13	92.86% (13/14)	0	0	0	11	100% (11/11)
ER-positive neuroendocrine tumor	luminal	0	0	0	6	100% (6/6)	0	0	0	6	100% (6/6)
triple-negative neuroendocrine carcinoma	triple negative	1	0	0	0	0% (0/1)	1	0	0	0	0% (0/1)
MC-MD	triple negative	0	0	1	5	100% (6/6)	2	2	0	1	20% (1/5)
invasive micropapillary carcinoma	luminal	0	0	0	1	100% (1/1)	0	0	0	1	100% (1/1)

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Table 7 Correlation of TRPS1 and AR expression in TNBC

| TNBC		AR		Total
		Intermediate and high positive	**Negative and low positive**	
TRPS1	Intermediate and high positive	338(34.88%)	538(55.52%)	876(90.40%)
	Negative and low positive	73(7.53%)	20(2.06%)	93(9.60%)
Total		411(42.41%)	558(57.59%)	969(100%)

The chi-square statistic is 54.828. The p value is < .001

and FOXC1 expression in 4 molecular types of breast cancer. The results demonstrated that TRPS1 had a significantly greater positivity rate than GCDFP-15 and FOXC1 in different molecular types of breast cancer ($p < 0.001$) (Fig. 3 and Table 8). Notably, FOXC1 had a greater positivity rate (71.98%) than GATA3 (53.57%) and GCDFP-15 (32.14%) and a lower rate than TRPS1 (93.13%) in TNBC.

Discussion

Special types of BC, representing 25% of all breast cancers, encompass a collection of different diseases characterized by different biological and pathological features, clinical presentations, responses to treatments, clinical behaviors, and outcomes [20]. We investigated TRPS1 expression in special types of BC, as mentioned in a few publications. TRPS1 is considered a "master controller"
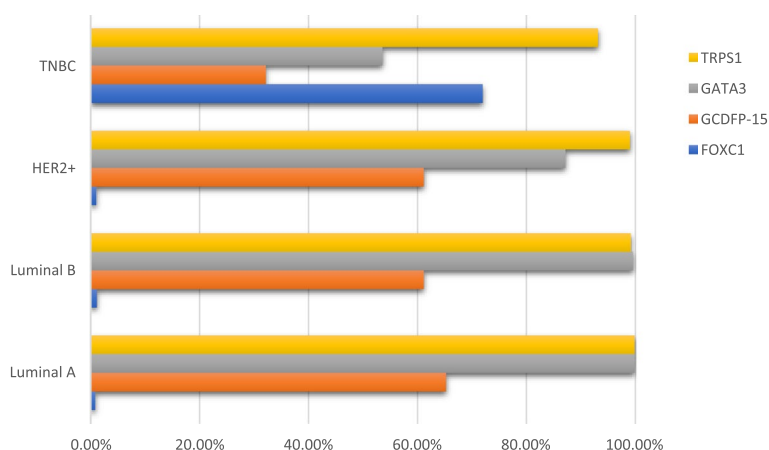
Fig. 3 The percentage of TRPS1, GATA3, GCDFP15 and FOXC1 expression among the four surrogate molecular types of invasive breast carcinoma

Table 8 Expression of TRPS1, GATA3, GCDFP-15 and FOXC1 in 4 molecular types of breast cancer

	TRPS1	GATA3	GCDFP-15	FOXC1
Molecular types of BC				
LuminalA	606/607(99.84%)	606/607(99.84%)	396/607(65.24%)	5/607(0.82%)
LuminalB	702/708(99.15%)	705/708(99.58%)	433/708(61.16%)	8/708(1.13%)
HER2 +	293/296(98.99%)	258/296(87.16%)	181/296(61.15%)	3/296(1.01%)
TNBC	339/364(93.13%)	195/364(53.57%)	117/364(32.14%)	262/364(71.98%)
Total	1940/1975(98.23%)	1764/1975(89.32%)	1127/1975(57.06%)	278/1975(14.08%)
P-value				
LuminalA	-	-	< .001	< .001
LuminalB	-	.504	< .001	< .001
HER2 +	-	< .001	< .001	< .001
TNBC	-	< .001	< .001	< .001

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of both luminal and basal differentiation, while GATA3 is a regulator and indicator of luminal differentiation. As predicted, TRPS1 and GATA3 were highly expressed in some special types of BCs, including mucinous carcinomas, invasive micropapillary carcinomas, tubular carcinomas and invasive lobular carcinomas, ER-positive neuroendocrine tumors and secretory carcinomas. In addition, TRPS1 was more highly expressed than GATA3 in AdCCs, MBCs and special metastatic types of BC. In triple-negative neuroendocrine carcinomas, TRPS1 and GATA3 were not expressed. In apocrine carcinomas, TRPS1 expression was lower than GATA3 expression.

According to the 5th WHO classification, breast neuroendocrine neoplasms are categorized as neuroendocrine tumors (mostly ER-positive), small cell neuroendocrine carcinomas or large cell neuroendocrine carcinomas. Our data demonstrated that TRPS1 and GATA3 expression was almost positive in ER-positive neuroendocrine tumors. However, triple-negative neuroendocrine carcinomas showed negative expression of TRPS1 and GATA3, similar to the findings of a previous study [15]. Previous studies have demonstrated that fibromatosis-like MBC is not sensitive to TRPS1 [10]. In our study, we found that TRPS1 was weakly positive in one patient with fibromatosis-like MBC. A larger sample of patients with fibromatosis-like MBC is needed to confirm the TRPS1 expression pattern. We also investigated TRPS1 expression in other MBCs, such as MC-MD and squamous cell carcinoma. All of these highly expressed TRPS1. Of the 7 patients with AdCC in our study, 3 had solid-basaloid adenoid cystic carcinoma, and the rest had classic adenoid cystic carcinoma. Our data revealed that TRPS1 expression was intermediate or highly positive in 100% of AdCCs. However, few studies have reported the opposite result of TRPS1 staining (2/5, 40%) in AdCC [15]. Another study showed that TRPS1 was positive in only 50% (3/6) classic AdCCs [21]. The main reason for this inconsistency is the small number of patients included in the previous study. TRPS1 was highly positive in SC, similar to that reported by others [15].

A previous study showed that TNBC with apocrine differentiation was predominantly negative for TRPS1 expression, while 82% of HER2 + IBC with apocrine differentiation exhibited negative TRPS1 expression [22]. Another study showed that in apocrine carcinomas, TRPS1 was negative in 4 patients (80%) and weakly positive in 1 patient (20%) [15]. Schwartz reported that TRPS1 was weakly expressed in a minority of triple-negative apocrine carcinoma tumors (3/14, 21%) [23]. These studies revealed low TRPS1 expression in AR-positive apocrine carcinoma. However, most of these studies included a relatively small number of apocrine carcinomas. In this study, we investigated

TRPS1 expression in a relatively large sample of 102 patients with apocrine carcinoma. A total of 63.73% of all patients were positive for TRPS1. In 77 patients with triple-negative apocrine carcinomas, 45 patients (58.45%) were positive for TRPS1. Among the 25 patients with HER2-positive apocrine carcinomas, 20 patients (80%) were positive for TRPS1. Relatively greater TRPS1 expression in apocrine carcinomas (especially those with a HER2-positive phenotype) was observed in our study than in previous studies. This could relate to some reasons, such as using of different antibody [24], different diagnostic thresholds for rendering a diagnosis of apocrine carcinoma. Our study included a relative high number of pure apocrine carcinomas All apocrine carcinomas included in our study were composed of > 90% apocrine differentiation components. Although the expression of TRPS1 in apocrine carcinomas in our study was greater than that in previous studies, it was still lower than that in other histological types, and the percentage of TRPS1-positive cells was lower than that of GATA3-positive cells in apocrine carcinoma. We also explored the correlation between TRPS1 and AR in TNBC. Our study showed that TRPS1 and AR expression was inversely correlated in TNBC.

TRPS1 has been found to be a highly sensitive marker for all breast cancer molecular types [10, 15, 25], consistent with our data. Our data showed an overall sensitivity of 93.13% (339/364) for TRPS1 expression in TNBCs. Parkinson et al. [10] reported that TRPS1 was highly expressed in TNBCs (97.4%). Ai et al. [26] reported that 86% of TNBCs were positive for TRPS1. These studies have provided further evidence suggesting that TRPS1 is highly important in TNBC. We evaluated TRPS1 expression in combination with other breast-specific markers (GATA3, GCDFP-15 and FOXC1) in a large cohort of breast cancer patients. FOXC1 is a reliable marker for TNBC. In addition, FOXC1 can serve as an additional diagnostic tool for triple-negative phenotypes and sub-classifications in TNBC [27]. Li reported that FOXC1 was positive in 77.84% of patients with TNBC [9]. Our study revealed that TRPS1 was more strongly expressed than GATA3, GCDFP-15 and FOXC1 in TNBC, and FOXC1 was more strongly expressed than GATA3 and GCDFP-15 in TNBC. However, some studies have raised concerns about the specificity of TRPS1. It has been reported that some prostate cancer and muscle invasive bladder cancers show significant staining [28]. Another report elucidated that TRPS1 was positive in non-breast tumors, such as soft tissue tumors, salivary gland tumors, squamous cell carcinomas, and gynecological cancers [29]. Additional comprehensive studies are needed to elucidate the true specificity of TRPS1 IHC staining for many

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tumor types before it is widely adopted in clinical practice. The combination of TRPS1 and FOXC1 could be recognized as a reliable diagnostic panel for identifying TNBC in clinical practice.

Conclusion

In conclusion, our study demonstrated that TRPS1 is a highly sensitive marker for most special types of breast carcinoma. TRPS1 was positive in 63.73% of apocrine carcinomas. TRPS1 and AR expression was inversely correlated in TNBC. TRPS1 was more highly expressed in 4 molecular types of breast cancer in Chinese patients. In TNBC, TRPS1 had a greater positivity rate than GATA3, GCDFP-15 and FOXC1.

Abbreviations

GATA3	GATA binding protein 3
GCDFP15	Gross cystic disease fluid protein 15
FOXC1	Forkhead box transcription factor C 1
TNBC	Triple-negative breast cancers
HER2	Human epidermal growth factor receptor 2
IBC	Invasive breast carcinoma
TRPS1	Trichorhinophalangeal syndrome type 1
MBC	Metaplastic breast carcinoma
AdCC	Adenoid cystic carcinoma
SC	Secretory carcinoma
AR	Androgen receptor
BC	Breast cancer
IHC	Immunohistochemistry
WHO	World Health Organization
ER	Estrogen receptor
PR	Progesterone receptor
ASCO/CAP	American Society of Clinical Oncology/College of American Pathologists
MC-MD	Metaplastic carcinoma with mesenchymal differentiation

Authors' contributions

All authors contributed to the study's conception and design. R.S., W.Y., Y.C., X.X., R.B., and B.Y. conducted patient recruitment and data collection. R.S. and C.K. drafted and revised the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study is in accordance with the Declaration of Helsinki and was approved by the ethics committees of Fudan University Shanghai Cancer Center. Informed consent forms have been obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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