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Research Article

TSPY Expression Identifies Higher-grade Breast Cancer in African American Women: Evidence of Fetal Microchimerism in Tumor Tissue

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Abstract

Fetal cell microchimerism, the presence of genetically distinct fetal cells in maternal tissues, arises naturally during pregnancy when fetal stem cells migrate into maternal circulation. These cells can engraft in damaged tissues, including malignancies, and may play a role in tumor biology. This study evaluated the association between fetal microchimerism—detected through Testis-Specific Protein Y-encoded (TSPY) expression—and clinicopathologic features of invasive breast cancer in African American women. We conducted a blinded case–case study using immunohistochemical analysis of TSPY expression in 202 archival breast cancer tissues. TSPY protein, a marker of microchimeric Y-chromosome DNA, was assessed in relation to clinical and pathological characteristics including estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) status, tumor grade, stage, size, and molecular subtype. Associations were examined using Chi-square tests. Survival outcomes were evaluated using Kaplan–Meier analysis. The results demonstrated that TSPY expression was not associated with patient age, receptor status, or triple-negative phenotype. However, TSPY positivity was significantly associated with higher tumor grade ($p = 0.043$), suggesting a relationship between fetal microchimerism and more aggressive disease features. Therefore, we concluded that microchimeric TSPY expression is enriched in higher-grade breast tumors among African American women. These findings suggest that fetal cell microchimerism may contribute to—or serve as a biomarker of—advanced breast cancer biology, although its mechanistic role requires further investigation.

Keywords

African American, Breast Cancer, Triple-negative, Microchimerism

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1. Introduction

Fetal-derived stem cells have been identified in the breast stroma, where they can proliferate, differentiate, and integrate into maternal tissues [1-4]. This phenomenon, known as fetal cell microchimerism, occurs naturally during pregnancy and results in the long-term persistence of genetically distinct fetal cells within the maternal host [5]. These cells have been detected in both normal and malignant breast tissues, suggesting a potential role in tissue remodeling and tumor biology.

Microchimeric cells have been hypothesized to contribute to the extensive epithelial expansion required for lactation during pregnancy, as well as to processes involved in tumor initiation and progression [6, 7]. Consequently, microchimerism may provide a biologically plausible mechanism underlying tumor aggressiveness, therapeutic resistance, and the high prevalence of triple-negative breast cancer (TNBC) among African American women.

Breast cancer remains a major public health concern, accounting for over 40,000 deaths annually in the United States [8]. Importantly, its clinical behavior varies across racial and ethnic groups. African American women are disproportionately affected by more aggressive disease, often presenting with higher-grade tumors, advanced-stage disease, and subtypes lacking targetable receptors [9, 10]. Breast cancer is a heterogeneous disease composed of multiple intrinsic molecular subtypes identified through gene expression profiling [11-13]. Among these, TNBC—defined by the absence of estrogen receptor (ER), progesterone receptor (PR), and HER2 expression is particularly aggressive and associated with poor prognosis due to limited therapeutic options [14, 15].

The role of microchimerism in breast cancer remains controversial. Some studies suggest that these cells may exert protective or reparative effects by contributing to tissue regeneration [16, 17], while others propose a tumorigenic role, potentially influencing cancer initiation and progression [18, 19]. Clarifying this duality requires evaluation of microchimerism in relation to tumor subtype and established prognostic factors.

In this study, we evaluated fetal microchimerism in breast tumors from African American women using immunohistochemical detection of testis-specific protein Y-encoded (TSPY), a marker of Y-chromosome-derived cells. We demonstrate that TSPY expression is significantly associated with higher tumor grade and shows an increasing trend with tumor size, although no association was observed with receptor status. These findings suggest that microchimerism may serve as a biomarker of aggressive breast cancer in this population.

2. Materials and Methods

2.1. Study Design

This study was reviewed and deemed exempt by the Howard University Institutional Review Board (IRB-15-MED-19). A total of 202 cases of invasive ductal carcinoma (IDC) from African American women diagnosed and treated at Howard University Hospital between 2000 and 2010 were included. Cases were selected based on the availability of adequate tumor tissue. Clinical and demographic data were obtained from the Howard University Cancer Center Tumor Registry.

2.2. Tissue Samples and Microarray Construction

Formalin-fixed, paraffin-embedded (FFPE) tumor specimens were used to construct tissue microarrays (TMAs) (Pantomics, Inc., Richmond, CA). Each TMA consisted of 1.0 mm cores sampled from representative tumor regions, with two cores per case. Sections (5 μm) were cut and mounted on microscope slides. Normal FFPE prostate tissue served as a positive control for TSPY expression.

2.3. Detection of Microchimerism

Microchimerism was assessed using immunohistochemistry (IHC) targeting TSPY, a Y-chromosome-encoded protein present in male cells. TSPY is highly repetitive within the Y chromosome and is considered a sensitive and reliable marker for detecting male microchimeric cells in female tissues [7, 20, 21].

2.4. Immunohistochemistry

Slides were deparaffinized, rehydrated, and subjected to heat-induced antigen retrieval (pH 9.0). Staining was performed using a rabbit polyclonal anti-TSPY antibody (Lifespan Biosciences) at an optimized concentration of 0.01 μg/mL on a Dako Autostainer system.

2.5. Scoring

TSPY expression was evaluated independently by two pathologists blinded to clinical data. An H-score system was used, with scores ≥200 classified as positive and <200 as negative.

2.6. Breast Cancer Subtypes

Tumors were classified into molecular subtypes based on ER, PR, HER2, and Ki-67 expression, following established criteria [12, 22].

2.7. Reagents

Antibodies used in this study were as follows: TSPY, and β-tubulin (Santa Cruz Biotechnology, Dallas, TX).

2.8. Culture of Breast and Prostate Cancer Epithelial Cell Lines

HCC70 (African American breast cancer), HCC1806 (African American breast cancer), and 22RV1 (metastatic resistant prostate cancer) epithelial cells were obtained from American Type Culture Collection (ATCC) (Manassas, VA). All three cell lines were maintained using advanced RPMI-1640 supplemented with 10% Fetal Bovine Serum (FBS), 100 U/ml penicillin, and 100mg/ml streptomycin at 37°C in a 5% CO2 atmosphere.

2.9. Western and Protein Isolation

HCC70, HCC1806, and 22RV1 epithelial cancer cells were cultured at 800,00 cells in 60 mm dishes for 24 hr. After 24 hr. protein cell lysates were collected with Solulyse-M Protein Extraction Reagent [a non-ionic detergent, 250 mM sucrose and 25mM Tris; pH 7.4] (Gentalis, San Diego, CA). Complete Mini Protease Inhibitor Cocktail was added to the lysis buffer. Protein extraction was performed according to the manufacturer's protocol. A total of 30 ug of protein was used for SDS-PAGE. 4-20% polyacrylamide gels (Biorad, Hercules, CA) were used to resolve proteins in SDS tris-glycine running buffer (1X) containing 25mM Tris, 192 mM glycine, and 0.1% (w/v) SDS, pH 8.3 (Biorad, Hercules, CA). The voltage was set to 100-115 volts to resolve the proteins. The proteins were transferred using an iBlot Transfer Device (LifeTechnologies, Carslbad, CA), which performed a dry transfer in 7 minutes at 20 volts. A polyvinylidene difluoride (PVDF) membrane located in iBlot Transfer Stacks (Life Technologies, Carslbad, CA) was used. Blocking buffer, antibody wash solution, primary diluent, and secondary diluent were prepared from components of WesternBreeze Chemiluminescent Immunodetection Kit (LifeTechnologies, Carslbad, CA) according to the manufacture's protocol. After the transfer was complete, membranes were blocked for 1 hour in 10 mL of blocking buffer at room temperature. Incubation of the membrane in blocking buffer and all other solutions were performed on a rocker at 60 rpm. Prior to the addition of diluted primary antibody, the membranes were washed 2 times for 2 minutes with distilled water. Membranes were incubated with primary antibody for an hour at room temperature or overnight at 4ºC. Membranes were washed 4 times for 5 minutes after primary antibody incubation period in antibody wash, followed by incubation with 10 mL of secondary antibody conjugated to horseradish peroxidase (HRP) (1:10,000) or alkaline phosphatase for 1 hour at room temperature. Anti-goat, anti-rabbit or anti-mouse alkaline phosphatase conjugated secondary antibodies were pre-made and provided in WesternBreeze Chemiluminescent Immunodection Kit. After secondary antibody incubation period, the membranes were washed with antibody wash 4 times for 5 minutes and then 2 times with distilled water before adding the appropriate chemiluminescent substrate. Supersignal West Femto Chemiluminescent substrate (Pierce of Thermo Scientific, Rockford, IL) was used for detection of secondary antibody conjugated to HRP. CDP-Star, from WesternBreeze Chemiluminescent Immunodetection Kit (Lifetechnolgies, Carlsbd, CA), was used as a substrate for secondary antibodies conjugated to alkaline phosphatase. Protein band detection and densitometry was acquired with ChemiDoc XRS+ Image Lab software (Biorad, Hercules, CA) using a charged coupled device (CCD) camera imager.

3. Statistical Analysis

Associations between TSPY expression and clinicopathologic variables were assessed using Chi-square tests. Survival analyses were conducted using Kaplan–Meier curves and log-rank tests. Statistical analyses were performed using SPSS version 22, with significance set at $p < 0.05$.

4. Results

4.1. TSPY Protein Expression Across Breast Cancer Histologies

TSPY protein expression was evaluated in control and tumor tissues, as illustrated in Figure 1. Positive staining was confirmed in normal prostate gland tissue (Figure 1A), validating assay specificity.

Across breast cancer specimens, TSPY expressions were observed in multiple histologic subtypes and tumor grades. High levels of TSPY expression were identified in grade 2 luminal A invasive ductal carcinoma (IDC) with calcifications and granulomatous features (Figure 1C), as well as in grade 2 luminal A (IDC) (Figure 1D). Elevated expression was also evident in more aggressive disease, including grade 3 IDC with Paget's disease (Figure 1E), grade 3 IDC with dense stromal fibrosis (Figure 1F), and grade 3 triple-negative IDC (Figure 1G).

Additionally, TSPY positivity was observed in grade 1 DCIS/IDC with fibrocystic changes and apocrine metaplasia, indicating that microchimerism may be present across both early and advanced lesions. In contrast, grade 3 triple-negative IDC with sclerosing adenosis demonstrated low or absent TSPY expression (Figure 1H), highlighting heterogeneity in microchimeric cell distribution.

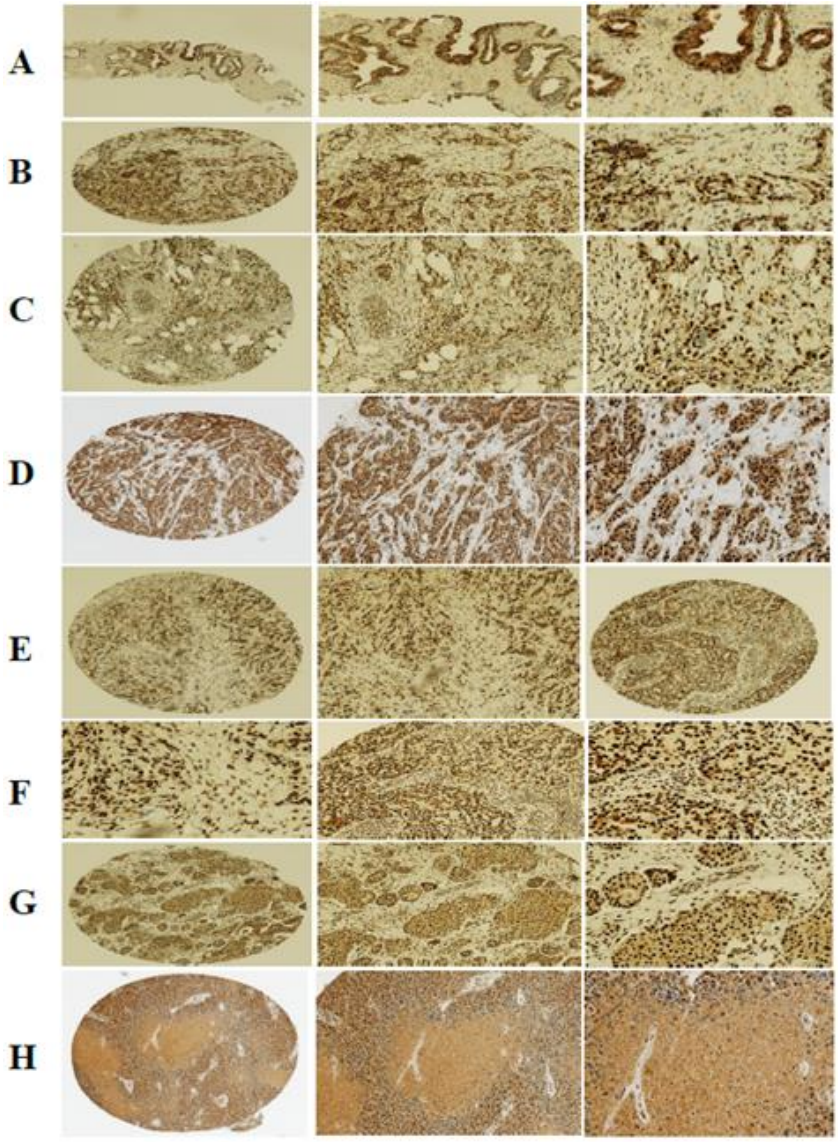

Figure 1. *TSPY protein expression in normal prostate and breast cancer tissues of varying grades and molecular subtypes. A) Normal Prostate Gland; B-C) Grade 2 Luminal A IDC; D) Grade 3 IDC with Pagets disease;. E) Grade 3 IDC Dense stromal fibrosis; F) Grade 3 triple negative IDC; G) Grade 1 DCIS/IDC; H) Grade 3 triple negative IDC with sclerosing adenosis. Representative images are shown at 4×, 10×, and 20× magnification.*

4.2. Association Between TSPY Expression and Clinicopathologic Features

Associations between TSPY expression and clinicopathologic parameters are summarized in Table 2. A statistically significant association was observed between TSPY expression and higher tumor grade ($p = 0.043$). Mean microchimeric cell counts increased from 243.17 ± 47.06 cells in grade 1–2 tumors to 257.60 ± 31.91 cells in grade 3 tumors, supporting a link between microchimerism and tumor aggressiveness.

Table 1. *Clinical and pathologic characteristics of study population with Breast Cancer.*

Population	Description	N	%
Age (years)			
	<50	57	28.2
	>50	145	71.8

Population	Description	N	%
ER status			
	Positive	49	39.2
	Negative	76	60.8
PR status			
	Positive	60	48.0
	Negative	65	52.0
HER2 status			
	Positive	112	89.6
	Negative	13	10.4
Subtype*			
	Luminal A	62	49.6
	Luminal B	14	11.2
	Her2	8	6.4
	Triple-negative	41	32.8
Stage at diagnosis			
	I	37	30.1
	II	50	40.7
	III	27	22.0
	IV	9	7.3
Size	<20mm	47	37.6
	20-50mm	42	33.6
	>50mm	19	15.2
	Unknown	17	13.6
Grade			
	1 and 2	41	32.8
	3	84	67.2
Distant Mets			
	None	105	84.0
	Distant Mets	20	16.0
Lymph Node Status			
	Negative	59	57.3
	Positive	44	42.7
Luminal			
	Not luminal	49	39.2
	Luminal	76	60.8
Triple Negative			
	Not triple negative	83	66.4
	Triple negative	42	33.6

Table 2. *Association of TSPY expression with clinicopathologic parameters of Breast Cancer.*

Breast Cancer Parameter	Description	TSPY Negative	TSPY Positive	*P*-value*
ER Status				
	Negative	6	43	
	Positive	8	68	.491
PR Status				
	Negative	7	53	
	Positive	7	58	.548
HER2				
	Negative	14	98	
	Positive	0	13	.196
Triple Negative				
	No	8	75	
	Yes	6	36	.310
Distant Metastases				
	No	12	93	
	Yes	2	18	.506
Subtype				
	Luminal A	8	54	
	Luminal B	0	14	
	Her2+	0	8	
	Triple-negative	6	35	.328
Stage at Diagnosis				
	I	4	33	
	II	7	43	
	III	3	24	
	IV	0	9	0.680
Size				
	<20mm	4	43	
	20-50mm	6	36	
	>50mm	0	19	.199
Grade				
	1+2 (ref)	8	33	
	3	6	78	.043
Lymph Nodes				
	Negative	8	51	
	Positive	4	40	.353
Luminal				
	Not Luminal	6	43	

Breast Cancer Parameter	Description	TSPY Negative	TSPY Positive	*P*-value*
	Luminal	8	68	.491
Tumor Size				
	T1	4 (40.0%)	43 (43.9%)	
	T2	6 (60.0%)	36 (36.7%)	
	T3	0 (0%)	19 (19.4%)	0.19

*based on χ^2 analysis and 1 df.

An increasing trend in microchimeric cell counts was also observed with tumor size, with mean values of 253.40 ± 44.42 cells for T1 tumors (<20 mm), 254.76 ± 36.59 cells for T2 tumors (20–50 mm), and 260.95 ± 21.94 cells for T3 tumors (>50 mm). However, this trend did not reach statistical significance (p = 0.199).

No significant associations were found between TSPY expression and ER status (p = 0.491), PR status (p = 0.548), HER2 status (p = 0.196), triple-negative status (p = 0.310), luminal subtype (p = 0.491), stage at diagnosis (p = 0.680), lymph node status (p = 0.353), or distant metastasis (p = 0.506). Mean microchimeric cell counts were 249.66 ± 45.08 cells in node-positive cases and 247.15 ± 27.63 cells in cases with distant metastasis.

4.3. Validation of the TSPY expression in breast cancer epithelial cells

To validate TSPY protein expression, we performed Western blot analysis using two African American breast cancer epithelial cell lines, HCC70 and HCC1806, with the 22RV1 castration-resistant prostate cell line serving as a positive reference control for TSPY expression (Figure 2). The HCC70 cell line was established from a 49-year-old Black female patient diagnosed with ductal carcinoma, whereas the HCC1806 cell line derived from a 60-year-old Black Female patient with primary acantholytic squamous cell carcinoma. The 22RV1 cell line, derived from a relapsed prostate tumor, is a well-established model of metastatic castration-resistant prostate cancer and was included as a comparator for TSPY expression.

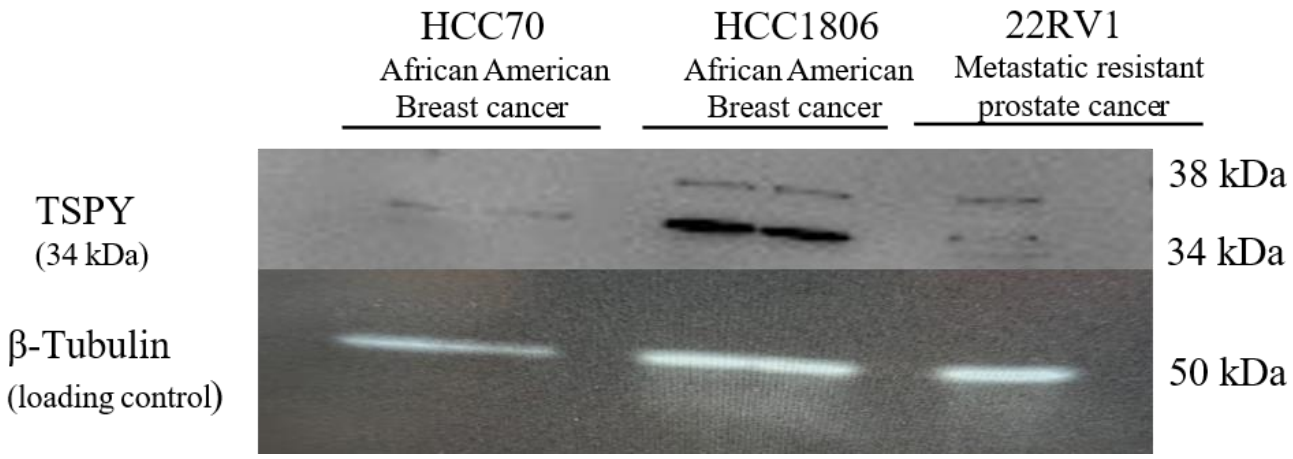

Figure 2. *Representative Western blot showing TSPY protein expression in HCC70, HCC1806, and 22RV1 cell lines. TSPY expression varied among cell lines, with highest expression in HCC1806, moderate expression in 22RV1, and minimal expression in HCC70. β-Tubulin served as the loading control.*

Western blot analysis demonstrated differential TSPY expression among the three cell lines. HCC1806 exhibited robust TSPY protein expression, whereas HCC70 displayed minimal expression. Similarly, the 22RV1 control cell line showed relatively low levels of TSPY expression. Equal protein loading was confirmed by total protein staining and β-Tubulin. These findings validate the expression of TSPY in advanced breast cancer epithelial cells and identify HCC1806 as a TSPY-expressing African American breast cancer model, supporting its utility for future mechanistic studies investigating the role of TSPY in breast cancer progression and tumor biology.

4.4. Survival Analysis

Overall survival (OS) and disease-free survival (DFS) were evaluated using Kaplan–Meier analysis (Figures 3 and 4). Median OS was 68.0 months (96% CI: 65.0–86.0) for tumors with low TSPY expression and 63.0 months (95% CI: 58.0–68.0) for TSPY-positive tumors, with no statistically significant difference observed (p = 0.15) (Figure 2).

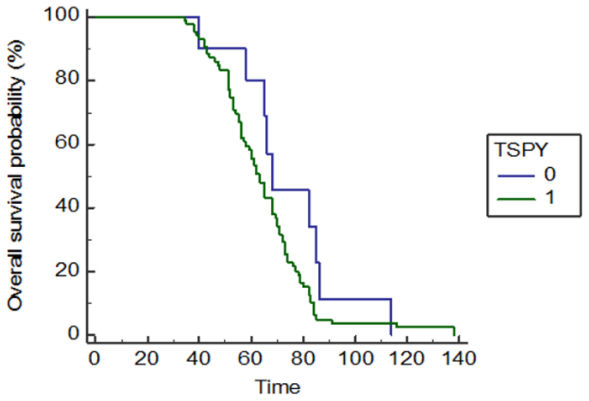

Figure 3. Image of Kaplan-Meier analysis of overall survival by TSPY expression (negative = 0, positive = 1) in breast cancer.

Similarly, TSPY expression was not significantly associated with DFS (p = 0.21) (Figure 3). The mean DFS was 89.17 months (95% CI: 64.57–113.77) in TSPY-negative tumors and 101.2 months (95% CI: 94.30–108.08) in TSPY-positive tumors.

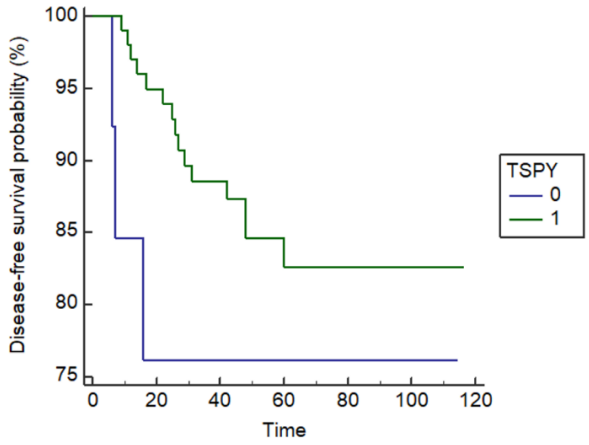

Figure 4. Kaplan–Meier analysis of disease-free survival by TSPY protein expression in breast cancer (recurrence = 1, no recurrence = 0).

5. Discussion

This study demonstrates that TSPY-detected microchimerism is significantly associated with higher tumor grade in breast cancer among African American women, a population disproportionately affected by aggressive disease. While prior studies have linked microchimerism to tumor presence, our findings extend this body of work by identifying a quantitative and statistically significant relationship between TSPY expression and tumor grade, suggesting a role in tumor progression rather than passive tissue integration [7, 23]. These findings are consistent with emerging evidence that pregnancy-acquired microchimerism represents a biologically important component of the tumor microenvironment. A recent systemic review and meta-analysis demonstrated that male-origin microchimerism is significantly associated with cancer risk while emphasizing substantial heterogeneity across tumor types and the need for tissue-based mechanistic studies [24]. Likewise, contemporary reviews suggest that fetal microchimeric cells may exert both tumor-protective and tumor-promoting effects depending on immune context, tissue environment, and cellular differentiation state [25].

A key contribution of this study is the focus on testis-specific protein Y-encoded (TSPY) as both a biomarker and a potential functional mediator. Increasing evidence indicates that TSPY plays an active role in oncogenesis. TSPY has been shown to regulate cell cycle progression through interactions with cyclin B/CDK1, promote cellular proliferation, and influence transcriptional programs associated with tumor growth [21, 26, 27]. More recent studies further suggest that aberrant TSPY expression contributes to tumorigenesis, genomic instability, and oncogenic signaling pathways in cancers such as prostate, hepatocellular carcinoma, and germ cell tumors [28-30]. These findings support a model in which TSPY-positive microchimeric cells may actively participate in tumor-promoting processes within the breast tumor microenvironment. Although most studies of TSPY have focused on prostate, germ cell, and hepatocellular malignancies, evidence indicates that cancer-testis antigens contribute to tumor plasticity, immune escape, and genomic instability across multiple solid tumors [28, 29]. Our findings suggest that TSPY may similarly identify biologically active microchimeric cells within aggressive breast cancers, extending its potential role beyond traditionally recognized TSPY-associated malignancies.

Importantly, TSPY expression in this cohort was not associated with ER, PR, HER2, or triple-negative status, suggesting that its relationship with tumor grade is independent of receptor-defined molecular subtypes. This observation implies that microchimerism may influence core tumorigenic processes, including proliferation, stromal remodeling, and immune modulation, rather than receptor-mediated signaling pathways. The observed trend toward increasing microchimeric cell counts with tumor size further supports a potential role in disease progression, although causality cannot be established from the current study.

The biological role of fetal microchimeric cells in cancer remains complex and is increasingly recognized as context dependent. While early investigations reported conflicting asso-

ciations between fetal microchimerism and breast cancer, recent evidence suggests that these cells may function as immune modulators, tissue repair progenitors, or contributors to tumor progression depending on the local microenvironment. A recent meta-analysis concluded that male-origin microchimerism demonstrates a significant association with cancer overall, while emphasizing the need to characterize the phenotype and functional properties of tissue-resident microchimeric cells [24]. Similarly, Parmeggiani et al. proposed that fetal microchimeric cells may transition between protective and tumor-promoting phenotypes in response to inflammatory and neoplastic signals [25]. Prior studies have demonstrated reduced circulating microchimerism in peripheral blood of breast cancer patients, suggesting recruitment and localization of these cells within tumor tissue [16, 31, 32]. One hypothesis is that tumors actively recruit microchimeric cells via chemokine-mediated homing mechanisms, similar to stem cell trafficking. Alternatively, microchimeric cells may initially contribute to tissue repair but undergo functional reprogramming within the tumor microenvironment, adopting pro-tumorigenic phenotypes that support angiogenesis, immune evasion, or stromal expansion [18, 33]. In this context, TSPY expression may identify a subset of microchimeric cells with enhanced proliferative or oncogenic potential.

These findings are particularly relevant to breast cancer disparities. Understanding the contribution of pregnancy-associated microchimerism to aggressive breast cancer may provide new insight into biologic mechanisms underlying disparities that are not explained by conventional molecular subtypes alone. Recent reviews have emphasized the need to investigate microchimerism across diverse populations because most published studies have involved predominately European cohorts [25]. African American women are more likely to develop high-grade, treatment-resistant tumors, yet the underlying biological drivers remain incompletely understood [10, 34]. Although TSPY expression was not associated with triple-negative status, its correlation with tumor grade suggests that it may serve as a complementary biomarker of aggressive disease, particularly in cases where traditional receptor-based classification provides limited prognostic value. Integration of microchimerism markers such as TSPY into existing biomarker panels may improve risk stratification and guide therapeutic decision-making.

From a translational perspective, TSPY and microchimerism represent promising areas for further investigation. TSPY detection could be incorporated into multiplex diagnostic platforms alongside established biomarkers. Moreover, if functional studies confirm a causal role, TSPY-associated pathways may provide novel therapeutic targets, particularly for aggressive tumors lacking conventional receptor targets. Additionally, characterization of microchimeric cell populations may offer new insights into tumor–host interactions, an emerging area of importance in cancer biology and immuno-oncology.

Several limitations should be considered. The use of Y-chromosome-based detection restricts analysis to male-derived fetal cells, excluding microchimerism from female pregnancies. The absence of parity data limits interpretation of the origin and persistence of these cells. RNA degradation in FFPE samples prevented transcript-level validation of TSPY expression and downstream signaling pathways. Furthermore, the case–case design precludes comparison with non-cancer controls, limiting causal inference. Despite these limitations, the observed association between TSPY expression and tumor grade supports the robustness and biological relevance of our findings.

Future studies should integrate multiplex immunohistochemistry, fluorescence in situ hybridization (FISH), digital PCR, single-cell RNA sequencing, spatial transcriptomics, and spatial proteomics to definitively identify TSPY-positive microchimeric cells and characterize their interactions with immune, stromal, and malignant cells. Recent reviews have identified these technologies as essential for determining whether fetal microchimeric cells function as tumor suppressors, tumor promoters, or biomarkers of disease progression [25, 35]. Incorporating parity data, longitudinal sampling, and functional assays will be essential to determine whether microchimeric cells are drivers of tumor progression, facilitators of tumor microenvironment remodeling, or biomarkers of disease evolution. Expanding these studies across diverse populations will also be critical to understanding the role of microchimerism in cancer disparities.

In conclusion, our findings demonstrate that TSPY-expressing microchimeric cells are associated with higher-grade breast cancer and may contribute to aggressive tumor biology. Collectively, these findings complement recent systematic reviews demonstrating the growing importance of pregnancy-associated microchimerism in cancer biology and identify TSPY as a promising biomarker of aggressive breast cancer. Future mechanistic studies are warranted to determine whether TSPY-expressing microchimeric cells represent active mediators of tumor progression or biomarkers of evolving tumor microenvironment.

6. Conclusion

In summary, our findings demonstrate that TSPY expression, a marker of fetal cell microchimerism, is not associated with age, hormone receptor status, or triple-negative breast cancer. However, TSPY expression shows a significant association with higher tumor grade, indicating a link with more aggressive disease.

These results suggest that fetal microchimerism may serve as a novel biomarker of advanced breast cancer, particularly in African American women who are disproportionately affected by high-grade tumors. While the underlying biological mechanisms remain to be fully elucidated, the association between TSPY expression and tumor aggressiveness highlights its potential clinical relevance.

Further studies integrating molecular and functional analyses are warranted to determine whether TSPY-positive microchimeric cells contribute directly to tumor progression or

reflect tumor–microenvironment interactions.

Abbreviations

ER	Estrogen Receptor
FPE	Formalin-Fixed, Paraffin-Embedded
FISH	Fluorescent in Situ Hybridization
HER2	Human Epidermal Growth Factor Receptor 2
IDC	Invasive Ductal Carcinoma
IHC	Immunohistochemistry
IRB	Institutional Review Board, Mets, Metastasis
PCR	Polymerase Chain Reaction
PR	Progesterone Receptor
SRY	Sex-Determining Region in the Y-Chromosome
SPSS	Statistical Package for the Social Sciences
TMA	Tissue Microarray
TNBC	Triple Negative Breast Cancer
TSPY	Testes Specific Y-Encoded Protein

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Author Contributions

Morgan Woods-Hooker: Conceptualization, Data curation, Writing – original draft

Tammy Naab: Formal Analysis, Resources, Visualization, Writing – review & editing

Luisel Ricks-Santi: Formal Analysis, Writing – review & editing

Desta Beyene: Formal Analysis, Methodology

Shreedhar Devkota: Methodology

Tamaro Hudson: Conceptualization, Data curation, Formal Analysis, Project administration, Resources, Supervision, Writing – original draft

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Conflicts of Interest

The authors declare no conflict of interest.

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