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Expression and Clinical Significance of FAM83A in Breast Cancer Tissues and Lymph Node Metastasis

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Abstract

Background To analyze the expression pattern of FAM83A and its clinical relevance in primary breast cancer tissues and corresponding lymph node metastases.

Method Firstly, 70 pathologically confirmed breast cancer specimens and 20 adjacent normal breast tissue samples were obtained from the Department of Breast Surgery of the Second Affiliated Hospital of Chengdu Medical College,Nuclear Industry 416 Hospital between January 2018 and December 2024. These 70 cancer specimens were categorized according to their lymph node metastasis status: 20 were from patients without lymph node metastasis and 50 from patients with lymph node metastasis. Additionally, another 20 breast cancer specimens with no lymph node metastasis were collected as blank controls. Subsequently, immunohistochemistry was performed to assess the expression level of FAM83A in all collected tissues.

Results Of the 70 breast cancer cases, 61 (87.1%) exhibited high FAM83A expression, including 41 (82%) of the 50 cases with lymph node metastasis.

Conclusion High FAM83A expression is correlated with breast cancer pathogenesis and may be implicated in lymph node metastasis.

1 Introduction

Breast cancer is the most commonly diagnosed malignancy and the leading cause of cancer-related death among women worldwide [1]. In the United States, mortality rates have declined by 42% since 1989, largely attributed to advancements in early detection and treatment [1]. However, breast cancer in China presents distinct epidemiological challenges, including a trend toward younger onset and a growing disease burden [2]. According to GLOBOCAN 2020, China is projected to account for approximately 491,000 new breast cancer cases and 176,000 deaths, with urban areas expected to have higher diagnosis rates than rural regions over the next decade [3]. These alarming statistics underscore the urgent need for efficient diagnostic biomarkers to enable early prevention and control.

Early detection remains critical for improving breast cancer prognosis. However, conventional imaging techniques such as X-ray mammography have inherent limitations, potentially delaying diagnosis in some patients. Consequently, the identification of tumor biomarkers has emerged as a focal point in breast cancer research, offering promise for early and accurate diagnosis [4]. The rapid advancement of bioinformatics and computational technologies has further accelerated this field, enabling deeper exploration of cancer-related genes [4].

One such gene of interest is FAM83A, a member of the FAM83 protein family. Characterized by a highly conserved N-terminal domain rich in serine and proline residues, FAM83A was initially classified as a member of the nitrilase-like family (family with sequence similarity 83, member A) before its oncogenic

potential was recognized [5]. Emerging evidence suggests that FAM83A and VEGF share consistent clinicopathological correlations in breast cancer and may represent potential therapeutic targets [6].

In this study, we utilized the GEPIA2 (Gene Expression Profiling Interactive Analysis 2) platform (http://gepia2.cancer-pku.cn/#index) to analyze FAM83A expression in breast cancer tissues. Our findings aim to provide important scientific evidence for elucidating the functional role of FAM83A in breast cancer pathogenesis.

2 Materials and methods

2.1 Expression data of FAM83A in breast cancer

We analyzed the expression level of the FAM83A gene in breast cancer using the GEPIA2 database (Gene Expression Profiling Interactive Analysis 2; http://gepia2.cancer-pku.cn/#index).

2.2 Patient information and clinical samples

Paraffin-embedded tissue blocks of primary breast cancer and matched lymph node metastases were obtained from our departmental tissue bank. All cases were independently reviewed and confirmed by two senior pathologists. Based on the following criteria, a total of 70 lesion samples were included. Inclusion criteria: (a) tissue samples from surgical resection; (b) treatment-naïve patients at first diagnosis; (c) complete clinical data available, with no age restriction. Exclusion criteria: (a) samples from core needle biopsy or fine-needle aspiration; (b) histologically ambiguous diagnoses; (c) patients who received neoadjuvant chemotherapy or any other anti-tumor therapy prior to surgery; (d) recurrent cases.

2.3 Methods

2.3.1 Sample Processing

All collected specimens were sectioned continuously in a single batch at a thickness of 4 μm and mounted onto clean, adhesive-coated slides, with at least five spare sections prepared per sample.

2.3.2 Immunohistochemical Staining (SP Two-step Method)

Paraffin sections were dewaxed, rehydrated, and rinsed with tap water. Antigen retrieval was performed according to the primary antibody specifications. Endogenous peroxidase activity was blocked by incubating the sections with peroxidase blocking reagent for 10 minutes at room temperature, followed by three 3-minute washes with PBS. After PBS removal, the sections were incubated with non-immune animal serum for 10 minutes at room temperature to block non-specific binding. The serum was then drained, and the sections were incubated with the primary antibody for 60 minutes at room temperature or overnight at 4°C, followed by three 3-minute PBS washes. Subsequently, the sections were incubated

with biotin-labeled secondary antibody for 10 minutes at room temperature and washed with PBS (3×3 minutes). Streptavidin-peroxidase reagent was then applied for 10 minutes at room temperature, followed by another PBS wash (3×3 minutes). Finally, freshly prepared DAB or AEC chromogen was applied for color development. The reaction was terminated by rinsing with tap water, and the sections were counterstained with hematoxylin, then blued with ammonia water.

2.3.3 Result Interpretation Criteria

Immunostaining was evaluated using the semi-quantitative scoring system proposed by Fromowitz. For each section, five high-power fields (×400) in cancer cell-rich areas were selected, and 100 cells per field were assessed. Staining intensity was scored as 0 (no color), 1 (light yellow), 2 (medium brown), or 3 (dark brown). The proportion of positively stained cells was scored as 0 (< 10%), 1 (10%–25%), 2 (26%–50%), 3 (51%–80%), or 4 (> 80%). A total score was calculated by summing the intensity and proportion scores. A total score of 0–1 was defined as negative, while a score of 2–7 was considered positive.

2.4 Statistical Methods

Statistical analysis was performed using SPSS 27.0. Categorical data were expressed as frequencies and percentages, and comparisons between groups were conducted using the chi-square test. A P-value < 0.05 was considered statistically significant.

3 Results

3.1 Analysis of the GEPIA2 database (http://gepia2.cancer-pku.cn/#index) revealed the expression profile of FAM83A across various tumor types. As shown in Fig. 1, FAM83A expression was significantly upregulated in breast cancer tissues.

3.2 The relationship between FAM83A expression and breast cancer

To determine the expression status of FAM83A in breast cancer, we quantitatively analyzed 70 paired breast cancer and adjacent normal tissue samples using immunohistochemistry. We observed a significant increase in FAM83A expression in cancer tissues (Fig. 2), and the detailed findings are summarized in Table 1.

Figure 2: A represents the conventional HE staining result of breast cancer, while B shows the IHC staining result of FAM83A in breast cancer.

Table 1: Expression of FAM83A in Breast Cancer Tissues

Table 1
Expression of FAM83A in Breast Cancer

	n	Positive	Weakly positive	Negative	Positive rate
FAM83A	70	61	4	5	87.1%

3.3 High FAM83A expression was observed in metastatic breast cancer nodules by immunohistochemical analysis, in contrast to normal lymph nodes (Fig. 3; Table 2).

Table 2: Expression of FAM83A in metastatic lymph nodes of breast cancer

Table 2
Expression of FAM83A in lymph node metastatic carcinoma tissues

	n	Positive	Weakly positive	Negative	Positive rate
FAM83A	50	41	4	5	82%

3.4 The Relationship between High Expression of FAM83A and Clinical and Pathological Characteristics of Breast Cancer

Analysis of the correlation between FAM83A expression and clinicopathological characteristics revealed that FAM83A levels were significantly elevated in breast cancer patients compared to controls ($p < 0.05$). Moreover, high FAM83A expression was significantly associated with lymph node metastasis and negative estrogen receptor status (both $p < 0.05$).

Table 3 The Relationship between High Expression of FAM83A and Clinical and Pathological Characteristics of Breast Cancer

Table 3
The Relationship between High Expression of FAM83A and Clinical and Pathological Characteristics of Breast Cancer

Clinical pathological characteristics: Breast cancer patients (n = 70)	**Clinical pathological characteristics: Breast cancer patients (n = 70)**		***P***	χ^2
Age, n (%)	Number (n)	FAM83A positive	1.026	0.311
<=60	49	44(89.7%)		
> 60	21	17(80.9%)		
T-stage, n (%)				
T1	32	26(81.25%)	3.356	0.34
T2	31	29(93.5%)		
T3	5	5(100%)		
T4	2	2(100%)		
N-stage, n (%)				
N0	38	34	3.843	0.279
N1	24	20		
N2	6	6(100%)		
N3	2	1(50%)		
M-stage, n (%)				
M0	20	0	4.131	0.042
M1	50	41(82%)		
Pathological stage, n (%)				
Stage I	35	29(82.9%)	1.444	0.695
Stage II	31	28(90.3%)		
Stage III	3	3(100%)		
Stage IV	1	1(100%)		
Histological type, n (%)				
Invasive ductal carcinoma	51	46(90.2%)	1.563	0.211
Invasive lobular carcinoma	19	15(78.9%)		
Size				
<=20mm	37	30(81.1%)	2.574	0.109

Clinical pathological characteristics: Breast cancer patients (n = 70)	Clinical pathological characteristics: Breast cancer patients (n = 70)		*P*	χ^2
> 20mm	33	31(94%)		
Progesterone status, n (%)				
Negative	18	16(88.9%)	1.163	0.559
Unclear	6	6(100%)		
Positive	46	39(84.8%)		
Estrogen status, n (%)				
Negative	21	21(100%)	11.08	0.004
Unclear	3	1(33.3%)		
Positive	46	39(84.5%)		
HER2 status, n (%)				
Negative	25	22(88%)	0.249	0.883
Unclear	5	4(80%)		
Positive	40	35(87.5%)		

4 Discussion

Breast cancer remains the most commonly diagnosed malignancy and a leading cause of cancer-related mortality among women worldwide [7]. In 2018, an estimated 1 million new cases were diagnosed globally, accounting for approximately one-quarter of all female cancers [11]. Despite significant advances in screening and treatment that have markedly improved patient survival, prognosis remains highly stage-dependent: the 5-year survival rate for stage I breast cancer approaches 100%, whereas for stage IV disease it plummets to approximately 26% [11]. This stark disparity underscores the urgent need for effective biomarkers to enable early detection and predict prognosis, particularly given the limited efficacy of conventional therapies—including surgery, chemotherapy, and radiotherapy—in advanced disease [12]. The complexity and heterogeneity of breast cancer further complicate treatment, and its underlying molecular mechanisms remain incompletely understood.

In this context, the identification of novel biomarkers is critical for improving diagnostic accuracy and therapeutic outcomes. Genes that are highly expressed in malignant tissues but show low or absent expression in benign lesions are of particular interest, as they may serve as both diagnostic indicators and therapeutic targets [8]. The FAM83 family member A (FAM83A), characterized by 83% sequence homology within its family [9], has emerged as one such candidate. Previous studies have reported its upregulation and functional significance in various malignancies, including lung, liver, and pancreatic

cancers, where it influences tumor growth, metastasis, invasion, and drug resistance [10]. However, its role in breast cancer, particularly in relation to lymph node metastasis, remains underexplored.

In the present study, we investigated FAM83A protein expression in 70 breast cancer tissues and 20 matched adjacent normal samples using quantitative immunohistochemistry. Our results demonstrated significantly elevated FAM83A expression in breast cancer tissues compared to normal controls, with particularly high levels observed in lymph node metastatic lesions. These findings align with bioinformatics analyses from the DGED database and SAG, which identified FAM83A as a breast cancer-associated gene [13]. The preferential upregulation of FAM83A in metastatic deposits suggests its potential involvement in tumor progression and dissemination, warranting further investigation.

Despite these promising findings, this study has several limitations. First, the sample size was relatively modest, and the absence of geographically and ethnically diverse populations may limit the generalizability of our conclusions. Second, while we established an association between FAM83A expression and lymph node metastasis, the precise molecular mechanisms through which FAM83A exerts its pro-metastatic effects remain to be elucidated. Third, the correlation between FAM83A expression levels and the number of metastatic lymph nodes—a critical prognostic factor—was not assessed. Finally, our study was limited to protein expression analysis and did not explore the broader regulatory network involving FAM83A.

Future research should address these gaps through several complementary approaches: (1) Large-scale, multi-center validation involving diverse populations to confirm the robustness of FAM83A as a prognostic biomarker; (2) Mechanistic studies to delineate the specific pathways by which FAM83A regulates breast cancer cell proliferation, migration, and invasion, particularly its role in mucinous breast cancer subtypes; (3) Clinicopathological correlation analyses examining the relationship between FAM83A expression levels, the number of involved lymph nodes, and patient outcomes including treatment response and survival; (4) High-throughput systems biology approaches, including gene expression profiling, proteomics, and bioinformatics, to map the FAM83A-centered regulatory network and identify upstream regulators and downstream effectors that may serve as additional therapeutic targets.

In conclusion, this study provides evidence that FAM83A is significantly upregulated in breast cancer tissues, particularly in cases with lymph node metastasis, positioning it as a promising novel biomarker for breast cancer progression. With further systematic investigation, FAM83A may not only deepen our understanding of breast cancer pathogenesis but also contribute to the development of targeted therapies and personalized treatment strategies, ultimately improving outcomes for patients with this devastating disease.

Declarations

Acknowledgements Not applicable.

Ethics approval and consent to participate

This study protocol related to human use has been complied with all the relevant national regulations, institutional policies and in accordance the tenets of the Helsinki Declaration, and has been approved by the Ethics Committee of the Second Affiliated Hospital of Chengdu Medical College, China National Nuclear Corporation 416 Hospital(YJ-2024-031).Consent for publication Informed consent was obtained for experimentation with human subjects.

Competing interests

The authors declare that they have no competing interests.

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Author Contribution

Shuaijun Zhang: concept and design.Jinrong Chen and Shigao Chen: collect specimens and corresponding clinical information.Jie Hu: clinical data analysis.Yulan Liu: draft the manuscript.All authors have read and agreed to the published version of the manuscript.

Data Availability

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

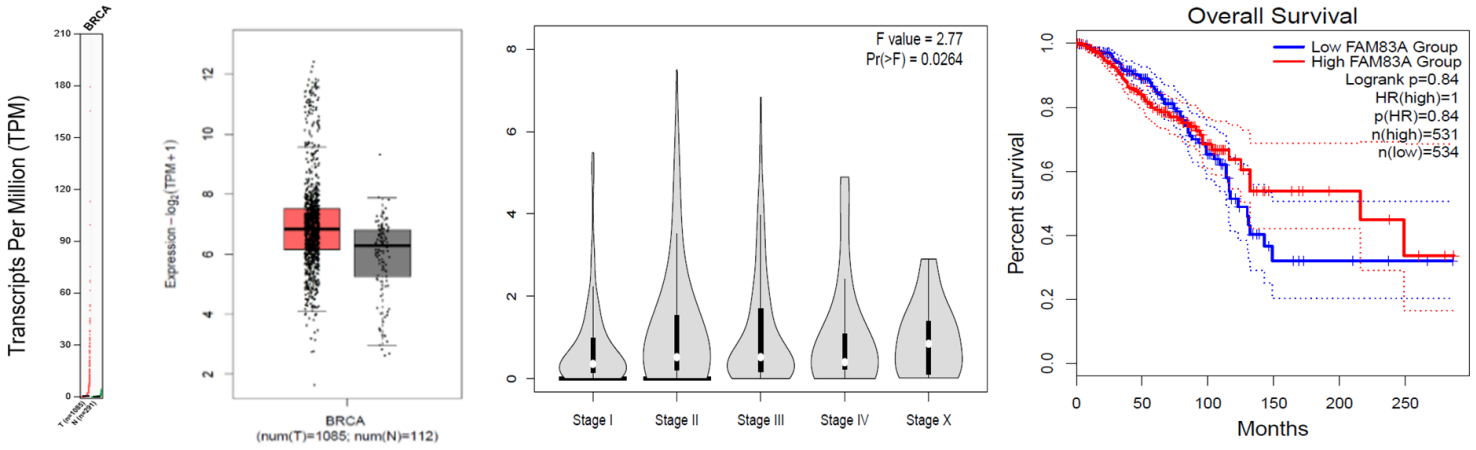


Figure 1

Bioinformatics analysis indicates the expression of FAM83A in breast cancer.

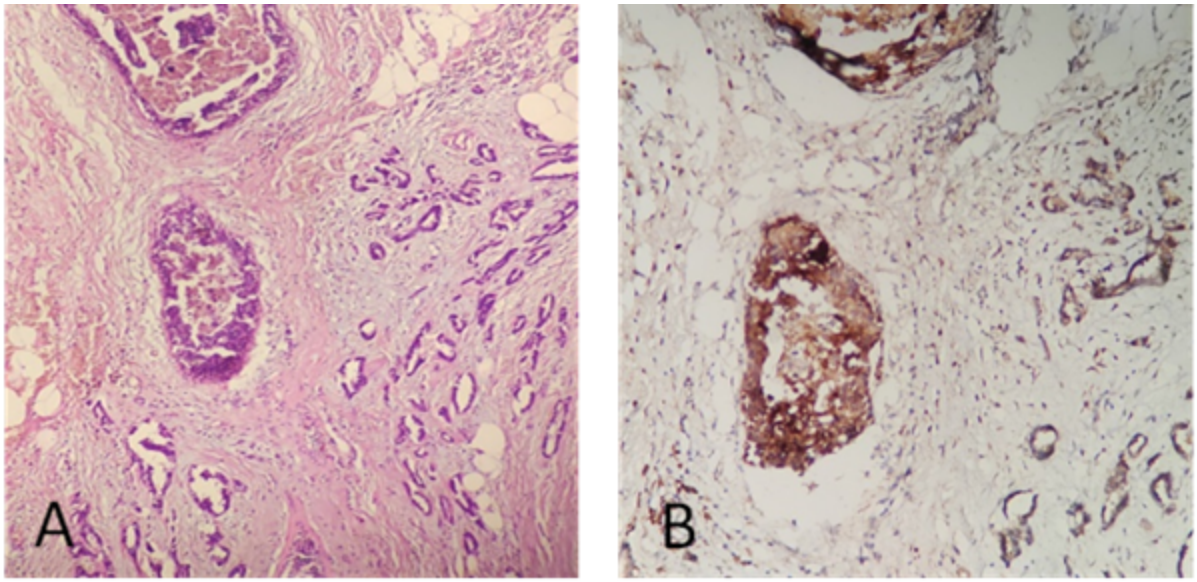


Figure 2

A represents the conventional HE staining result of breast cancer, while B shows the IHC staining result of FAM83A in breast cancer.

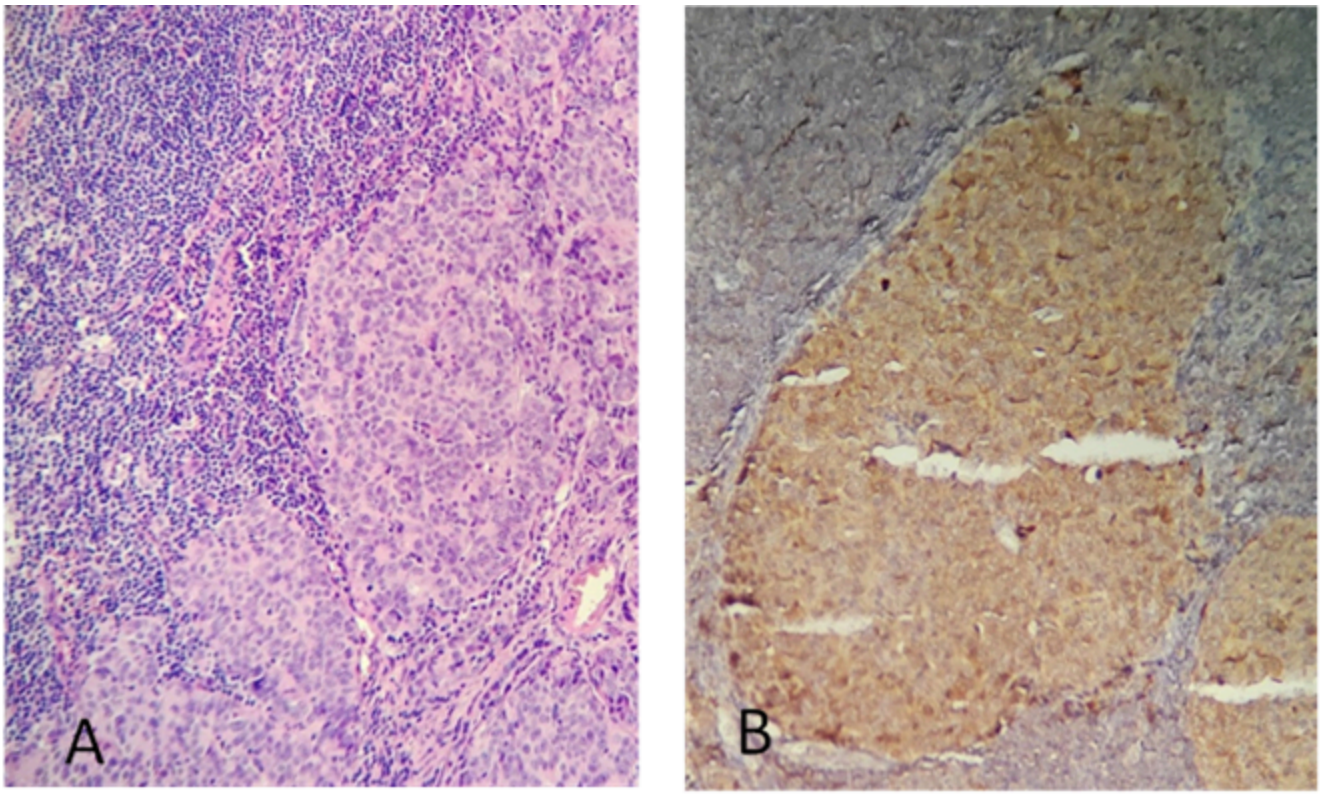


Figure 3

A represents the conventional HE staining of lymph nodes from breast cancer metastasis, while B shows the IHC staining result of FAM83A in lymph nodes from breast cancer metastasis.