International Journal of Medical and Pharmaceutical Research

Online ISSN-2958-3683 | Print ISSN-2958-3675
Frequency: Bi-Monthly
Available online on: https://ijmpr.in/

Original Article

Immunohistochemical Expression of Survivin and Cd44 in Er, Pr, Her 2-Neu +/- Cases of Carcinoma Breast- A Correlative Study

Dr Priyanka Sharma[1], Dr Nishi Tandon[2], Dr Andleeb Zehra[3], Dr Farheen Khan[4], Dr Moniza Ilyas[5], Dr Nirupma Lal[6]

[1]MD pathology (Postgraduate Resident) Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India
[2]MD Pathology (Professor)Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India
[3]MD Pathology (Assistant Professor) Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India
[4]MD pathology (Postgraduate Resident) Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India
[5]MD Pathology Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India
[6]MD Pathology (Professor & Head) Department of Pathology, Era Lucknow Medical College and Hospital, Lucknow, India

OPEN ACCESS

Corresponding Author:

Dr Nishi Tandon
Department of Pathology Era Lucknow Medical College and Hospital, Lucknow – 226003, India
Email: drnishitandon@gmail.com

Received: 20-02-2026
Accepted: 08-03-2026
Available online: 05-04-2026

ABSTRACT

Breast carcinoma remains one of the leading causes of cancer-related morbidity and mortality among women worldwide. Recent advances in immunohistochemistry have emphasized the importance of identifying novel biomarkers that may improve prognostic accuracy and therapeutic targeting. Survivin, an inhibitor of apoptosis, and CD44, a cancer stem cell marker, have emerged as significant contributors to tumor progression and resistance mechanisms. The present study aimed to evaluate the immunohistochemical expression of Survivin and CD44 in breast carcinoma cases and to correlate their expression with established markers, including estrogen receptor (ER), progesterone receptor (PR), and HER2/neu status. This study was conducted on histopathologically confirmed cases of breast carcinoma. Immunohistochemical staining was performed, and expression patterns were analyzed. The findings demonstrated variable expression of Survivin and CD44 across different receptor profiles. Increased expression of these markers was associated with more aggressive tumor characteristics and unfavorable receptor status. In conclusion, Survivin and CD44 may serve as valuable adjunct biomarkers in breast carcinoma, aiding in better understanding tumor biology and potentially guiding targeted therapeutic strategies.

Keywords*: Survivin, CD44, Breast carcinoma, Immunohistochemistry, ER PR HER2.*

INTRODUCTION

Breast carcinoma is the most frequently diagnosed malignancy among women worldwide and remains a leading cause of cancer-related mortality. Recent global estimates indicate a rising incidence, particularly in developing countries such as India, where a substantial disease burden exists due to late presentation and limited access to screening programs.[1]

Breast cancer demonstrates significant heterogeneity in its histopathological features, molecular profile, and clinical behavior. Conventional prognostic factors such as tumor size, lymph node involvement, and histological grading provide valuable information but are often insufficient to fully predict tumor progression and therapeutic response. Consequently, immunohistochemical markers including estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2/neu) have become essential in clinical decision-making.[2]

Despite these advances, certain subtypes—particularly triple-negative breast carcinoma—pose therapeutic challenges due to the absence of targeted treatment options. This has led to increasing interest in identifying additional biomarkers that may improve prognostic assessment and guide therapy.[3]

Survivin, a member of the inhibitor of apoptosis protein family, plays a crucial role in tumor development by inhibiting programmed cell death and promoting cell proliferation. Overexpression of survivin has been reported in various malignancies and is often associated with poor clinical outcomes.[4]

CD44 is a transmembrane glycoprotein involved in cell adhesion, migration, and tumor progression. It is also considered a marker of cancer stem cells and has been implicated in tumor invasion, metastasis, and resistance to therapy.[5]

However, limited studies have explored the correlation of survivin and CD44 expression with established hormonal receptors in breast carcinoma. Therefore, the present study was undertaken to evaluate their immunohistochemical expression and assess their relationship with ER, PR, and HER2/neu status.

MATERIALS AND METHODS

The present study was a cross-sectional observational study conducted in the Department of Pathology at Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh, India, over a period of 24 months (from November 2023 to October 2025). A total of 63 patients aged between 30 and 80 years, who were clinically suspected and subsequently confirmed as cases of breast carcinoma on histopathological examination, were included in the study. Only cases with adequate formalin-fixed paraffin-embedded (FFPE) tissue blocks were considered suitable for inclusion, while cases with poorly preserved tissue samples or incomplete clinical and histopathological data were excluded to ensure accuracy and reliability of the results.

All tissue specimens were fixed in 10% neutral buffered formalin, processed using routine histopathological techniques, and embedded in paraffin. Sections of 3–5 µm thickness were cut and stained with hematoxylin and eosin for microscopic evaluation and confirmation of diagnosis using standard methods.[6]

Immunohistochemical analysis was performed on representative paraffin-embedded tissue sections using antibodies against estrogen receptor (ER), progesterone receptor (PR), HER2/neu, survivin, and CD44. ER and PR expression were assessed based on nuclear staining and interpreted using the Allred scoring system.[7] HER2/neu expression was evaluated by assessing the intensity and completeness of membranous staining in accordance with the ASCO/CAP guidelines.[8] Survivin expression was analyzed based on nuclear and/or cytoplasmic staining patterns as described in previously published studies,[4] while CD44 expression was assessed based on membranous staining intensity and its distribution in tumor cells.[5]

For interpretation, both the proportion of positively stained tumor cells and staining intensity were recorded. Based on these parameters, cases were categorized as positive or negative according to established criteria.[4–5]

All collected data were compiled and analyzed using Statistical Package for the Social Sciences (SPSS). Descriptive statistics were applied, and appropriate statistical tests were used to assess the correlation between survivin and CD44 expression with hormonal receptor status (ER, PR, and HER2/neu). A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 63 histopathologically confirmed cases of breast carcinoma were included in the present study. The age of the patients ranged from 30 to 80 years, with a mean age of 48.65 ± 11.19 years. The majority of patients belonged to the 40–50 years age group, accounting for 33.3% (n=21), followed by 50–60 years in 25.4% (n=16). The 30–40 years and 60–70 years age groups each contributed 19.0% (n=12), while only 3.2% (n=2) of patients were aged between 70 and 80 years.

The study population showed a marked female predominance, with females constituting 93.7% (n=59) of cases, whereas males accounted for only 6.3% (n=4).

On histopathological evaluation, infiltrating ductal carcinoma (NOS) was the most common subtype, observed in 95.2% (n=60) of cases. Metaplastic spindle cell carcinoma was seen in 3.2% (n=2), while cribriform carcinoma was identified in 1.6% (n=1), indicating that invasive ductal carcinoma was overwhelmingly the predominant histological type (**Table 3**).

According to Nottingham grading, the majority of tumors were classified as Grade II, accounting for 47.6% (n=30) of cases. This was followed by Grade III tumors in 39.7% (n=25), while Grade I tumors were observed in only 12.7% (n=8). Lymph node involvement was present in 55.6% (n=35) of cases, indicating regional metastasis, while 44.4% (n=28) of cases showed no lymph node involvement (**Table 3**).

Based on pathological staging, the majority of tumors were classified as pT3, accounting for 49.2% (n=31), followed by pT4b in 41.3% (n=26), pT2 (6.3%, n=4), and pT4c (3.2%, n=2). With respect to nodal staging, pN2a was the most frequent category (66.7%, n=42), followed by pN0 (20.6%, n=13), pN3a (7.9%, n=5), and pN1a (4.8%, n=3).

Evaluation of hormone receptor status revealed that estrogen receptor (ER) and progesterone receptor (PR) positivity were each observed in 61.9% (n=39) of cases, while 38.1% (n=24) were negative. HER2/neu positivity was seen in 79.4% (n=50), while 20.6% (n=13) were negative (**Table 3**).

Based on molecular classification, the majority of cases belonged to the Luminal B subtype (50.79%, n=32), followed by HER2-enriched subtype (28.57%, n=18), Luminal A subtype (11.11%, n=7), and triple-negative subtype (9.52%, n=6). This distribution is illustrated in **Figure 1**.

Assessment of Survivin expression demonstrated that strong expression was the most common pattern, observed in 50.8% (n=32) of cases, followed by medium expression in 23.8% (n=15), while moderate and weak expression were each observed in 12.7% (n=8) of cases. Representative microphotographs showing Survivin expression across different tumor grades are depicted in **Figures 2–4**.

CD44 expression analysis revealed weak expression in 39.7% (n=25), moderate expression in 36.5% (n=23), and strong expression in 23.8% (n=15). Representative images of CD44 expression in different grades are shown in **Figures 5–7**.

When Survivin expression was analyzed in relation to tumor characteristics, a statistically significant association was observed with tumor (T) stage (χ^2=18.71, p=0.028), indicating higher expression with increasing tumor size. However, no significant association was found with Nottingham grade (p=0.939), nodal stage (p=0.713), or lymph node status (p=0.704). Similarly, CD44 expression did not show a statistically significant association with Nottingham grading (p=0.887), tumor stage (p=0.493), nodal stage (p=0.817), or lymph node status (p=0.315).

Analysis of Survivin expression in relation to hormone receptor status showed no statistically significant difference in overall expression between receptor-positive and receptor-negative groups for ER (p=0.224), PR (p=0.224), or HER2/neu (p=0.445).

However, when Survivin intensity was evaluated, a statistically significant association was observed with ER and PR status (χ^2=11.66, p=0.009), as detailed in **Table 1**. No significant association was found with HER2/neu status (p=0.799).

CD44 expression showed a statistically significant association with ER (p=0.029) and PR (p=0.029), but not with HER2/neu status (p=0.321).

A strong and statistically significant association was observed between Survivin and CD44 expression (χ^2=28.43, p<0.001), as shown in **Table 2**. Cases with strong Survivin expression demonstrated a higher proportion of strong CD44 expression, indicating a positive correlation between the two markers.

Further receptor-wise analysis demonstrated statistically significant associations between Survivin and CD44 expression in ER-negative (p=0.019), ER-positive (p=0.007), PR-negative (p=0.019), PR-positive (p=0.007), and HER2-positive cases (p=0.002), while no significant association was observed in HER2-negative cases (p=0.083).

Table 1: Association of Survivin Expression with Hormone Receptor Status

Receptor	Weak n (%)	Moderate n (%)	Medium n (%)	Strong n (%)	χ^2	p-value
ER Negative (n=24)	6 (25.0%)	0 (0%)	8 (33.3%)	10 (41.7%)	11.66	0.009*
ER Positive (n=39)	2 (5.1%)	8 (20.5%)	7 (17.9%)	22 (56.4%)		
PR Negative (n=24)	6 (25.0%)	0 (0%)	8 (33.3%)	10 (41.7%)	11.66	0.009*
PR Positive (n=39)	2 (5.1%)	8 (20.5%)	7 (17.9%)	22 (56.4%)		
HER2 Negative (n=13)	2 (15.4%)	2 (15.4%)	4 (30.8%)	5 (38.5%)	1.01	0.799
HER2 Positive (n=50)	6 (12.0%)	6 (12.0%)	11 (22.0%)	27 (54.0%)		

Table 2: Association of Survivin Expression with CD44 Expression

Survivin Expression	CD44 Weak n (%)	CD44 Moderate n (%)	CD44 Medium n (%)	CD44 Strong n (%)	Total (%)
Weak	8 (12.7%)	6 (9.5%)	3 (4.8%)	8 (12.7%)	25 (39.7%)
Moderate	0 (0%)	2 (3.2%)	4 (6.3%)	17 (27.0%)	23 (36.5%)
Strong	0 (0%)	0 (0%)	8 (12.7%)	7 (11.1%)	15 (23.8%)

Table 3: Key Clinicopathological Characteristics

Variable	Number (n=63)	Percentage (%)

IDC (NOS)	**60**	**95.2%**
Grade II	**30**	**47.6%**
Grade III	**25**	**39.7%**
Lymph node positive	**35**	**55.6%**
ER positive	**39**	**61.9%**
HER2 positive	**50**	**79.4%**

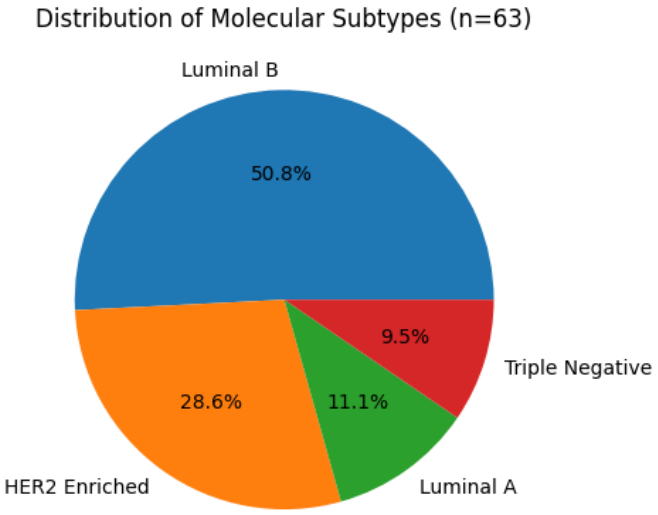

Figure 1: Distribution of molecular subtypes of breast carcinoma.

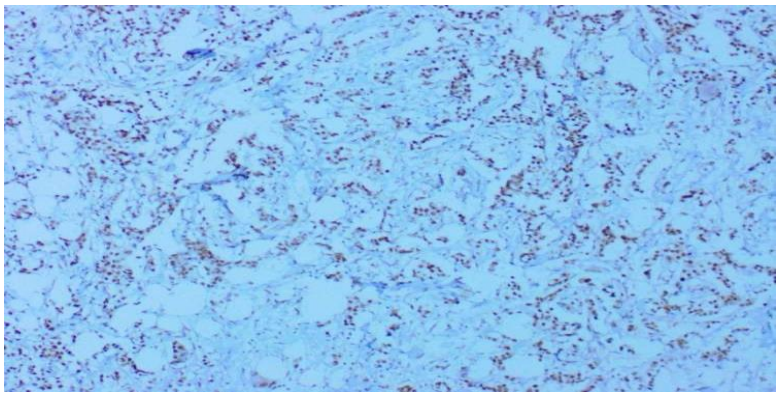

Fig 2 : Survivin positivity in Grade I carcinoma breast (100x)

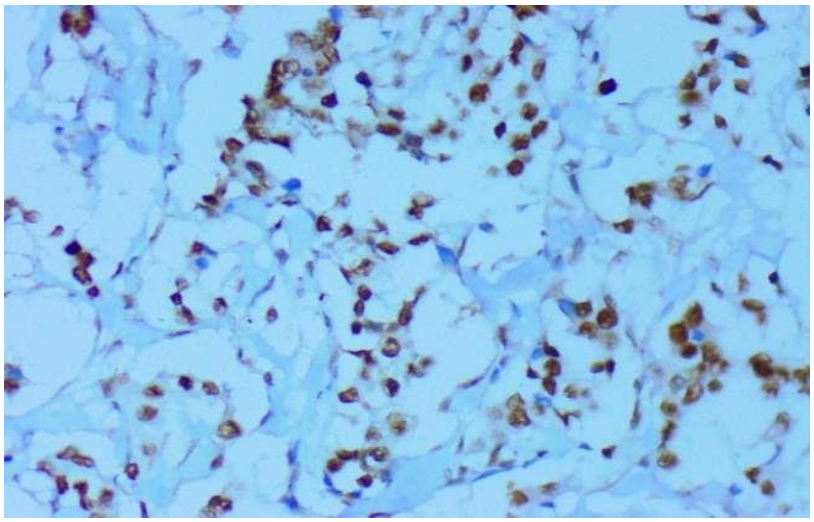

Fig 3 : Survivin positivity in Grade II carcinoma breast (400x)

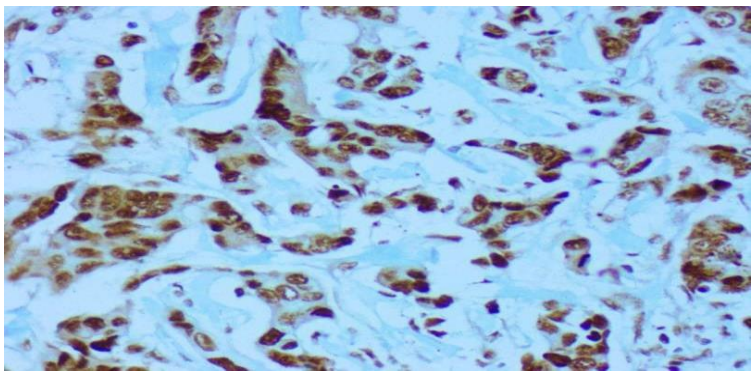

Fig 4 : - Survivin positivity in Grade III carcinoma breast (400x)

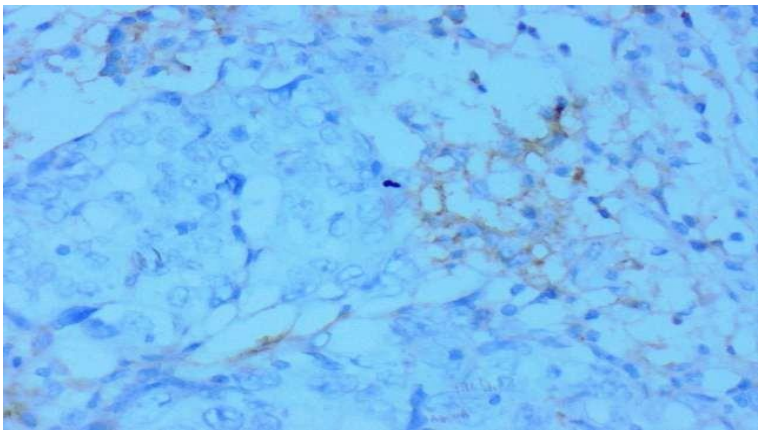

Fig 5 : CD44 positivity in Grade I carcinoma breast (400x)

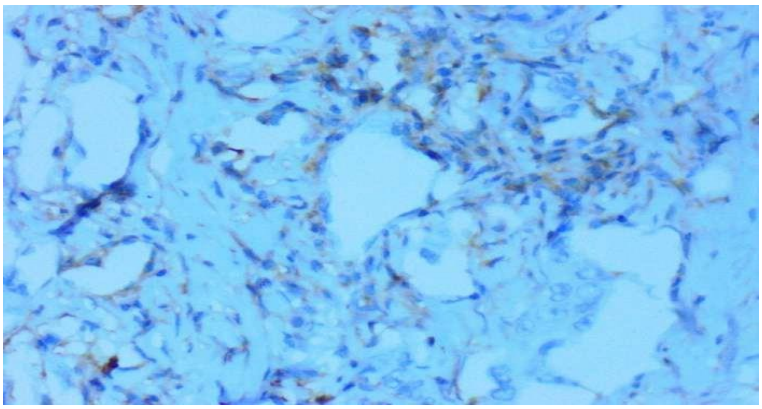

Fig 6 : CD44 positivity in Grade II carcinoma breast (400x)

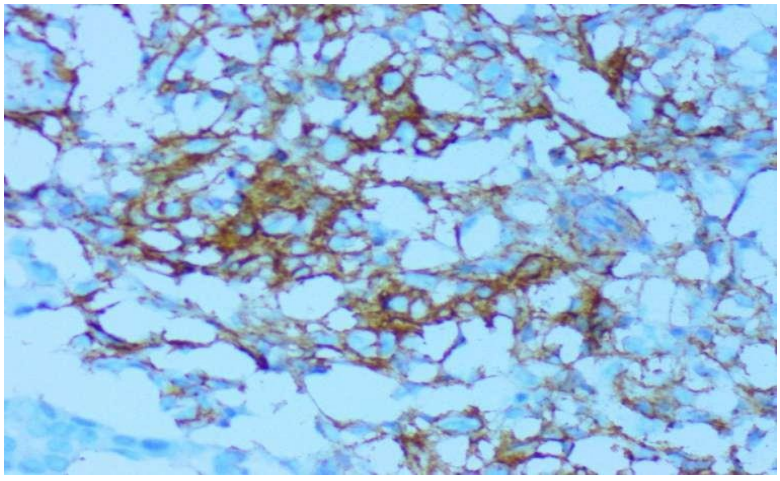

Fig 7 : CD44 positivity in Grade III carcinoma breast (400x)

DISCUSSION

The present study evaluated the immunohistochemical expression of survivin and CD44 in breast carcinoma and analyzed their association with clinicopathological parameters and hormone receptor status. The key findings of this study include a high prevalence of survivin expression, significant association of survivin intensity with ER and PR status, and a strong positive correlation between survivin and CD44 expression.

Survivin, a member of the inhibitor of apoptosis protein family, has been widely studied for its role in tumor progression and resistance to apoptosis. In the present study, survivin expression was observed in all cases, with strong expression seen in the majority. Similar findings have been reported by Altieri et al., who demonstrated that survivin is highly expressed in various malignancies and is associated with aggressive tumor behavior.[9] Likewise, Jha et al. reported increased survivin expression in breast carcinoma and its association with higher tumor grade and poor prognosis.[10] However, in contrast to some studies that demonstrated a significant association between survivin expression and tumor grade, the present study did not find a statistically significant correlation with Nottingham grading, suggesting variability across different populations.[11]

The association of survivin expression with tumor stage observed in the present study is consistent with previous reports. Tanaka et al. demonstrated that survivin expression increases with advancing tumor stage and is associated with tumor progression.[12] This finding supports the role of survivin in promoting tumor growth and survival, particularly in advanced stages of disease.

In the present study, survivin expression did not show a statistically significant association with ER, PR, or HER2 status when considered as a whole. However, survivin intensity showed a significant association with ER and PR positivity. Similar observations have been reported by Kennedy et al., who found that higher survivin expression levels are associated with hormone receptor-positive tumors.[13] In contrast, some studies have reported higher survivin expression in hormone receptor-negative tumors, indicating heterogeneity in tumor biology.[14]

CD44, a cell surface glycoprotein and cancer stem cell marker, plays a crucial role in tumor invasion, metastasis, and resistance to therapy. In the present study, CD44 expression showed a statistically significant association with ER and PR status but not with HER2 status. Similar findings have been reported by Abraham et al., who demonstrated that CD44 expression correlates with hormone receptor status and may serve as a marker of tumor aggressiveness.[15] However, other studies have reported an association of CD44 with triple-negative breast carcinoma, highlighting differences in study populations and methodologies.[16]

A major finding of the present study is the strong and statistically significant association between survivin and CD44 expression. This suggests a possible interaction between anti-apoptotic mechanisms and cancer stem cell pathways in breast carcinoma. Similar correlations have been described in previous studies, where co-expression of survivin and CD44 was associated with increased tumor aggressiveness and poor clinical outcomes.[17] These findings indicate that survivin and CD44 may act synergistically in promoting tumor progression and resistance to therapy.

The biological explanation for these findings may lie in the role of survivin in inhibiting apoptosis and regulating cell division, while CD44 contributes to tumor cell adhesion, migration, and maintenance of cancer stem cell properties. Together, these markers may enhance tumor survival, proliferation, and metastatic potential, thereby contributing to disease progression.[18]

From a clinical perspective, the evaluation of survivin and CD44 expression may provide additional information beyond conventional prognostic markers. Their combined assessment may help in identifying high-risk patients and could potentially serve as targets for novel therapeutic strategies.

However, the present study has certain limitations. The sample size was relatively small, and the study was conducted at a single center, which may limit the generalizability of the findings. Additionally, long-term follow-up data were not available to assess the prognostic significance of these markers.

CONCLUSION

The present study demonstrates that survivin is consistently expressed in breast carcinoma and shows a significant association with tumor stage and hormone receptor status, particularly ER and PR. CD44 expression also correlates with hormone receptor positivity, suggesting its role in tumor behavior. The strong association observed between survivin and CD44 expression indicates a possible interplay between anti-apoptotic pathways and cancer stem cell mechanisms in breast carcinoma.

These findings highlight the potential utility of survivin and CD44 as adjunct biomarkers in understanding tumor biology and identifying patients with more aggressive disease. However, further large-scale studies with long-term follow-up are required to establish their definitive prognostic and therapeutic significance.

REFERENCES

1. Bancroft JD, Gamble M. Theory and practice of histological techniques. 7th ed. Churchill Livingstone; 2013.
2. Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer. Mod Pathol. 1998;11:155–168.
3. Wolff AC, Hammond MEH, Hicks DG, et al. Recommendations for HER2 testing in breast cancer. J Clin Oncol. 2013;31:3997–4013.
4. Altieri DC. Survivin in cancer biology and therapy. Nat Rev Cancer. 2008;8:61–70.
5. Zöller M. CD44: structure and function in cancer progression. Nat Rev Cancer. 2011;11:254–267.
6. Bancroft JD, Gamble M. Theory and practice of histological techniques. 7th ed. Churchill Livingstone; 2013.
7. Allred DC, Harvey JM, Berardo M, Clark GM. Prognostic and predictive factors in breast cancer. Mod Pathol. 1998;11:155–168.
8. Wolff AC, Hammond MEH, Hicks DG, et al. Recommendations for HER2 testing in breast cancer. J Clin Oncol. 2013;31:3997–4013.
9. Altieri DC. Survivin, cancer networks and pathway-directed drug discovery. *Nat Rev Cancer*. 2008;8:61–70.
10. Jha K, Shukla M, Pandey M. Survivin expression and its prognostic significance in breast carcinoma. *Indian J Pathol Microbiol*. 2012;55:488–493.
11. Ryan BM, O'Donovan N, Duffy MJ. Survivin: a new target for anti-cancer therapy. *Cancer Treat Rev*. 2009;35:553–562.
12. Tanaka K, Iwamoto S, Gon G, et al. Expression of survivin and its relationship to loss of apoptosis in breast carcinomas. *Clin Cancer Res*. 2000;6:127–134.
13. Kennedy SM, O'Driscoll L, Purcell R, et al. Prognostic importance of survivin in breast cancer. *Br J Cancer*. 2003;88:1077–1083.
14. Span PN, Sweep CG, Wiegerinck ET, et al. Survivin is an independent prognostic marker for risk stratification of breast cancer patients. *Clin Chem*. 2004;50:1986–1993.
15. Abraham BK, Fritz P, McClellan M, et al. Prevalence of CD44+/CD24− cells in breast cancer. *Cancer Res*. 2005;65:10946–10951.
16. Al-Hajj M, Wicha MS, Benito-Hernandez A, et al. Prospective identification of tumorigenic breast cancer cells. *Proc Natl Acad Sci USA*. 2003;100:3983–3988.
17. Kim YS, Lee JW, Kim YS, et al. Co-expression of survivin and CD44 in breast carcinoma and its clinical significance. *Oncol Rep*. 2010;24:123–129.
18. Zöller M. CD44: can a cancer-initiating cell profit from an abundantly expressed molecule? *Nat Rev Cancer*. 2011;11:254–267.