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The Detailed Study of CD10: A Stromal Marker in Breast Carcinoma

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Breast carcinoma is one of the most frequently occurring cancers among women with one million cases. Breast cancer is the primary cause of death in women around the world. It is one of the major concerns in public health due to its high occurrence and growing tendency. This complex functional structure develops from a highly modified apocrine sweat gland in the female, but remains rudimentary in male. Breast develops embryological into two lines along milk lines extending from axilla to groin. CD-10 is a 90- to 110-kDa cell surface zinc dependent metalloproteinase which is known as "Common Acute Lymphoblastic Leukaemia Antigen" (CALLA). CD-10 acts as a stem cell regulator in the breast and prevents uncontrolled proliferation on stem cells The present study is designed to study the expression of CD-10, a breast carcinoma stromal marker and its correlation with ER, PR and HER2/neu status in breast carcinoma.

Keywords: Breast carcinoma; CD-10 a stromal marker; apocrine sweat gland.

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1. INTRODUCTION

The National cancer registry programme in its 2011 report [1,2,3] states that breast cancer is the commonest cancers among women in India with a regular annual increase [4]. Globally, breast cancer is considered as the frequently occurring non-skin cancer in females [5]. It is anticipated to become over two million annually by the year 2030. Recent researches point to the fact that breast cancer has been more among the women in the age group 25-45 years [1]. In socioeconomically underprivileged countries and in India, most women seek medical care only when the disease has progressed to advanced stages resulting in poor prognosis with a survival rate of just five years [6-8]. Due to meticulous research over the last few decades noted advances has been developed in the field of breast cancer treatment [8-10]. If breast cancer is detected at its early stages then its progression can be predicted more clearly and its management becomes comparatively easier [11]. Early diagnosis also gives a better outcome for women living with the disease. The clinical, pathological and molecular features with diverse prognostic and therapeutic implications have helped in understanding breast cancer to be more than a single disease. Its diverse biological subtypes with distinct natural history makes it a multifaceted disease [12-15].

Breast tissue is composed of duct (epithelial origin) and stroma (mesenchymal origin). Epithelial growth of tumour depends partly on chemical mediators between tumour cells and stromal cells [16]. CD10 is a myoepithelial marker [17]. In Invasive ductal carcinoma of breast CD10 loss in myoepithelial cell and CD10 expression in stromal cells denotes transition from epithelial to mesenchymal (EMT) and is associated with aggressive behavior [18,19]. Recently it has been suggested that changes occurring at the gene level in stroma can elevate carcinogenesis [20]. CD-10 is a zinc dependent metalloproteinase found on the cell surface and is also known as “Common Acute Lymphoblastic Leukaemia Antigen” (CALLA). Being a stem cell regulator in breast, this 90-110 kDa metalloproteinase regulates the uncontrolled proliferation in stem cells [21]. Although breast cancer mainly affects the epithelia, the modulation of tumor invasion and metastasis is regulated by stroma. Studying the contribution of stroma to the progression of cancer seems worth exploring as it will help in identifying markers specific to growth promotion, dedifferentiation, invasion, and ectopic survival of tumor cells and may in the course of time help identify new therapeutic targets for future treatment [22]. There were no correlations between stromal CD10 expression, age, tumour size, histological grade or clinical stage.CD 10 positive subgroup of patient also had a shorter metastatic free survival, and CD10 was the single significant prognostic factor for overall survival in the unvariate analysis [23-25]. These results suggested that stromal expression of CD10 in breast cancer is an important novel prognostic factor

2. MATERIALS AND METHODS

The study was conducted in the Department of Pathology, for the duration of two years from September 2015 to September 2017. This is a prospective study in which 50 samples of breast carcinoma by clinical and histomorphological method are included in the study.

Patient details such as age, clinical presentations, stage of the disease, radio diagnosis were obtained from the requisition form sent by clinicians and the details of pathological aspects like gross findings etc. are noted. The patients were selected based on following inclusion and exclusion criteria.

2.1 Inclusion Criteria

- Age from 21-80 years
- Patients with invasive breast carcinoma irrespective of type, grade diagnosed by histopathology in the department.
- Invasive breast carcinoma irrespective of nodal metastasis or not
- Patient irrespective of whether axillary dissection done for lymph node status or not.
- Mastectomy, Modified Radical Mastectomy, Lumpectomy, Core biopsy specimen received in the department of pathology.

2.2 Exclusion Criteria

- Age less than 21 and more than 80 years.
- Breast carcinoma in situ irrespective of type diagnosed by Histopathology.
- Those patients who have not given consent
- Male patients.

The final study population included 50 patients, who are diagnosed with breast carcinoma which included patients aged 21 to 80 years, who has undergone mastectomy procedure after obtaining informed written understandable consent. The specimen were received to pathology department in 10% neutral buffered formalin. After adequate fixation, the gross morphology of the specimens was recorded with total submission of breast samples and representative bits were taken from mastectomy specimens. After tissue processing, 5-7um thick sections were stained with haematoxylin and eosin and were studied microscopically. Relevant clinical data was collected from the hospital and laboratory records.

2.3 Statiscal Analysis

The data was statistically analyzed using Microsoft Excel and SPSS version 23. The significance of the results was assessed by determining the probability factor "P" value using the chi- square tests.

P<0.01 = highly significant
P<0.05 = significant
P>0.05 = Not significant

3. RESULTS

This 2 year study (from September 2015) was conducted by the combined effort of the Department of Pathology and the Department of Surgery, Sree Balaji Medical College and Hospital, Chennai. A total of 50 cases of formalin fixed paraffin embedded breast tissue were analyzed for 3 traditional markers ER, PR and Her2neu and correlated them with CD10 stromal positive cases.

Age distribution: The above Figure shows the distribution of age in the breast carcinoma cases chosen for study. It is evident that majority of the cases are in the 40-60 years age group with a mean age of 52.28 years and a standard deviation of 11.97.

The shows pie-chart shows categorization of the histopathological types of breast carcinoma.

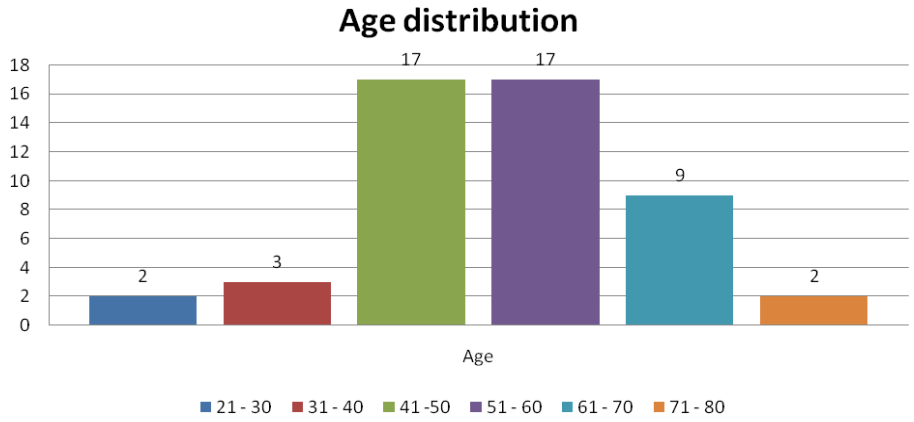

Fig 1. Distribution of cases by age group

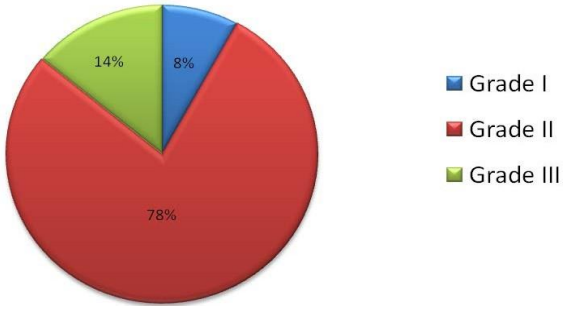

Fig 2. Distribution of cases by histological grade

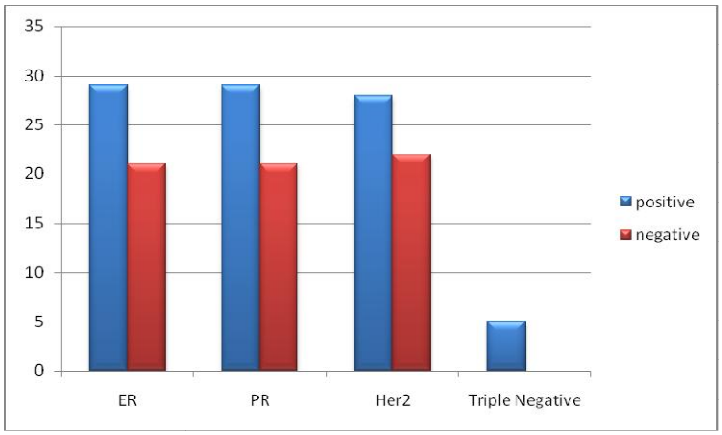

Fig. 3. Number of breast carcinoma cases that are ER, PR and HER2/neu receptor positive/negative

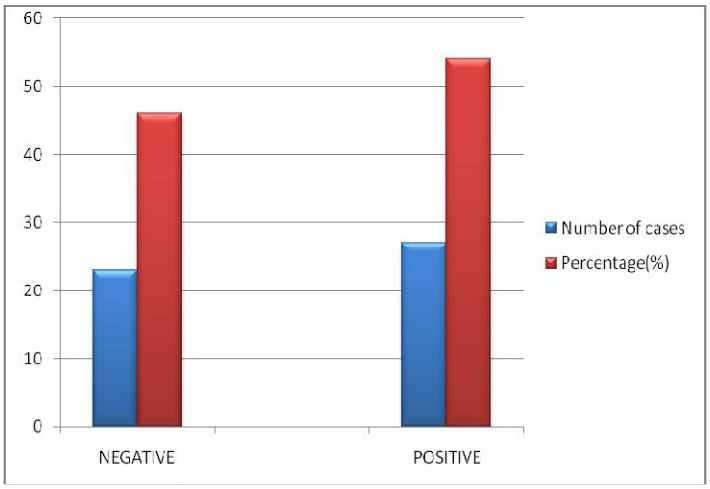

Fig. 4. Number of cases with degree of CD10 expression

Fig. 5. Specimen of Modified Radical Mastectomy showing a well circumscribed tumor

Fig. 6. Specimen of Modified Radical Mastectomy showing a well circumscribed tumour

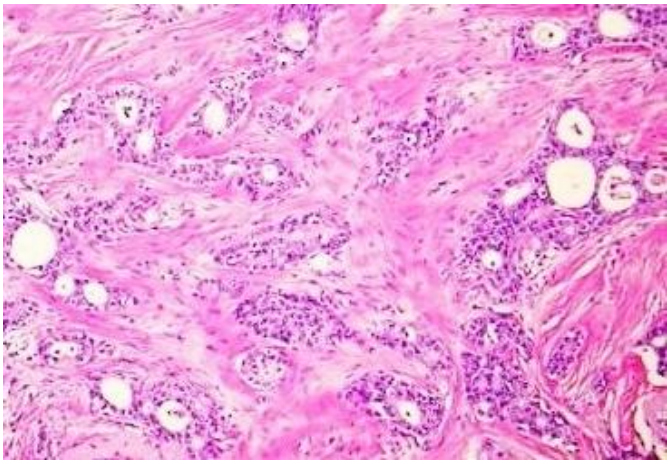

Fig. 7. IDC-NOS Grade I (H&E, 10X)

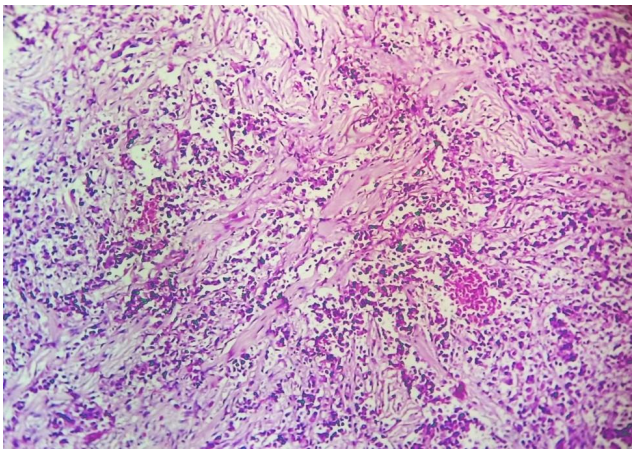

Fig. 8. IDC-NOS Grade II (H&E, 10X)

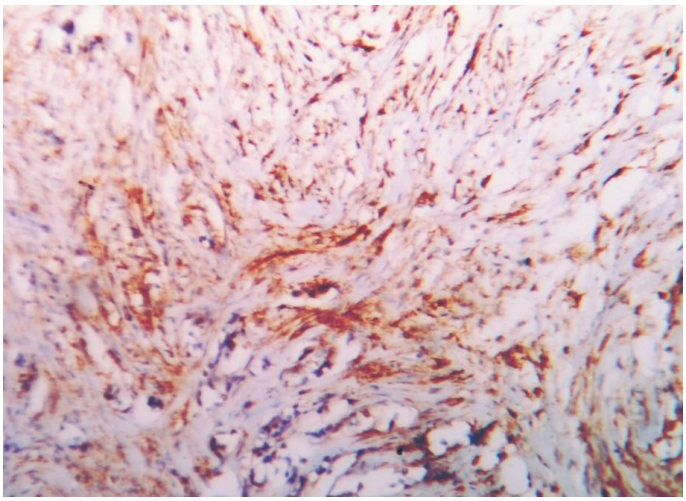

Fig. 9. Showing stromal positivity (IHC,10X)

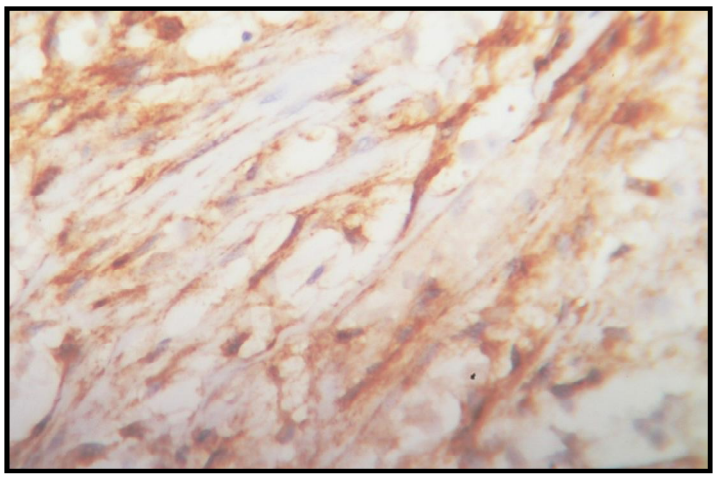

Fig. 10. Showing stromal positivity (IHC,40X)

4. DISCUSSION

Stromal cells play an key role in the development and metastasis of breast carcinoma. Tissue microenvironment plays a crucial role in regulating the survival, proliferation, migration, polarization, and differentiation of a cell. Being a zinc dependent surface neutral endopeptidase, CD10 causes the degradation of different bioactive peptides. Moreover, acting as a stem cell regulator in breast, this 90-110 kDa metalloproteinase regulates the uncontrolled proliferation in stem cells. The secretions by tumourous stromal cells affects the continous bilateral interaction at the molecular level between normal epithelial cells and stromal cells. The matrix metalloproteinase (MMP) is one such factor. Elevated MMP activities correlate with poor prognosis and promotes tumourigenesis , angiogenesis, invasion and metastasis .

In the present study it was detected that invasive ductal carcinoma occurs mainly in the age group of 21 to 80 years with a mean age of 52 years. Yamaguchi et al. [26], in his study, states that invasive ductal carcinoma breast were predominant in 27 to 87 years age group with the mean age being 52. Invasive ductal breast carcinoma occurs in the age group od 25-70 years with a mean age of 50. These findings by Yamaguchi et al and Putti et al substantiate the

results found in the present study. . The tumour size in the present study ranged from 2 – 10cm in maximal diameter with 62% showing tumour size less than 5cm in maximal diameter. In accordance with this result, Van der Vegt et al, [27] and Lu et al. and Huidrom Jyotsna Devi [28,29] reported that 93.5% and 89% of the cases selected in their studies, showed tumour sizes less than 5 cm (maximal diameter), respectively. As observed in the present study the correlation between the tumour size and CD10 expression was also insignificant in other studies (Makretsov, et al. [16], In this study, positive lymph node metastasis was seen in all invasive duct carcinoma grade III patients, whereas all invasive duct carcinoma grade I patients were negative. In invasive duct carcinoma grade II patients, a slight predominance of lymph node negativity (53.9%) was seen. However, a significant association between stromal CD10 immunostaining intensity and lymph node metastasis was not attained. Makretsov et al. [16] also found that the lymph node status did not influence the CD10 immunostaining intensity. The results seen in the breast carcinoma cases of the present study show clearly that 8 % belong to grade I, 78% belong to grade II and 14% belong to grade III. In corroboration with this result, Makretsov et al [16] and Yamaguchi et al [26] showed that the majority of invasive breast carcinoma cases belonged to the Grade II category with 53.8% and 40% showing invasive breast carcinoma.

The insignificance in the correlation between stromal CD10-positive immunostaining and tumor histological grade ($P>0.05$) seen in the present study may be attributed to the small sample size. In the present study 54% (27 out of 50) of the cases were positive for CD10 in the stroma. Similarly, found CD 10 expression in 55% (16 out of 29) cases. 79% (205 out of 258) and 80% (40 out of 50) of invasive breast carcinomas were reported by Makretsov et al. [16] When more than 10% of the stromal cells in vicinity of the neoplastic epithelial cells, CD10 expression may be considered positive. This criteria helped in detecting stromal CD10 expression in 19% of IDC. The correlation between CD10 and ER/PR negativity was good and statistically significant. A few studies also substantiate this finding showing statistically significant correlation between strong CD10 positive staining and ER/PR negativity.

Additionally a significant correlation was also observed between CD10 immunostaining intensity and HER2/neu expression. In support of this finding in the present study similar results were reported.

5. CONCLUSION

CD10 was found to have good correlation with ER/PR negativity and was statistically significant. To conclude, CD10, a stromal marker should be used in conjunction with ER/PR and Her2/neu Immunohistochemistry to predict the outcome in breast carcinoma for probable diagnostic therapy in future. Further studies need to be done to study the role of CD10 in breast carcinoma in invasion and metastasis.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

The study was approved of the Ethical committee, SBMCH (Sree Balaji Medical college and Hospital).

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, et al. Fact Sheets by Cancer [Internet]. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11 [Internet]. Lyon, France: International Agency for Research on Cancer. 2013;2013:4.
2. De Santis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. CA Cancer J Clin. 2014;64:52–62.
3. Dsouza NDR, Murthy NS, Aras RY. Projection of cancer incident cases for

India - Till 2026. Asian Pacific J Cancer Prev [Internet]. 2013;14(7):4379– 86.

4. Okonkwo QL, Draisma G, Der Kinderen A, Brown ML, De Koning HJ. Breast cancer screening policies in developing countries: A cost-effectiveness analysis for India. J Natl Cancer Inst. 2008;100(18):1290–300.
5. Kumar V, Abbas AK, Fausto N, Aster JC. Robbins and Cotran Pathologic Basis of Disease, Professional Edition: Expert Consult-Online [Internet]. Robbins and Cotran Pathologic Basis of Disease. 2009;487- 528.
6. Dury RAB, Wallington EA C. Histopathological techniques. 5th ed. Oxford New York. 1980;140-141.
7. Mott JD, Werb Z. Regulation of matrix biology by matrix metalloproteinases. Current Opinion in Cell Biology. 2004;16: 558–64.
8. Fidler IJ. Timeline: The pathogenesis of cancer metastasis: The seed and soil hypothesis revisited. Nat Rev Cancer [Internet]. 2003;3(6):453–8.
9. Jinga DC, Blidura A, Condrea I, Ardeleanu C DC. MMP -9 and MMP -2 gelatinases and TIMP-1 and TIMP-2 inhibitors in breast: Ccoarnrceelration with prognostic factors. J Cell Mol Med. 2006;10:499–510.
10. Putti TC, El-Rehim DMA, Rakha EA, Paish CE, Lee AH, Pinder SE, et al. Estrogen receptor-negative breast carcinomas: A review of morphology and immunophenotypical analysis. Mod Pathol [Internet]. 2005;18(1):26–35.
11. Scully OJ, Bay B-H, Yip G, Yu Y. Breast cancer metastasis. Cancer Genomics Proteomics [Internet]. 2012;9(5):311–20.
12. Wheaters's Functional Histology A Text and Colour Atalas. Wheaters's Functional Histology A Text and Colour Atlas. 6TH Edit.
13. Rosen PP, Hoda SA, Brogi E, Koerner FC. Rosen's Breast Pathology; 2014.
14. Inderbir Singh. Human Embryology. 10th editi. New Delhi : Jaypee Brothers Medical Publishers; 2014.
15. David G Hicks, Susan Carole Lester. Diagnostic pathology. Breast. Second edi. Philade lp: Hia, PA Elsevier; 2016.
16. Makretsov NA, Hayes M, Carter BA, Dabiri S, Gilks CB, Huntsman DG. Stromal CD10 expression in invasive breast carcinoma correlates with poor prognosis, estrogen receptor negativity, and high grade. Mod Pathol [Internet]. 2007;20(1):84–9.
17. Kalof AN, Tam D, Beatty B CK. Immunostaining patterns of myoepithelial cells in breast lesions: A comparison of CD10 and smooth muscle myosin heavy chain. J Clin Pathol. 2004;57:625-9.
18. Prabhakaran C Arun. CD10 as a prognostic stromal marker in Breast Carcinoma. J Dent Med Sci. 2017;16(1): 119–22.
19. Swayamprava Pradhan, Chandan Bajad DPMS. J. Evid. Based Med. Health. Stromal Expr cd10 invasive breast carcinoma its Correl with known Progn markers. 9(4):4243–53.
20. Cunha GR, Hayward SW, Wang YZ, Ricke WA. Role of the stromal microenvironment in carcinogenesis of the prostate. International Journal of Cancer. 2003;107:1–10.
21. Finak G, Bertos N, Pepin F, Sadekova S, Souleimanova M, Zhao H, et al. Stromal gene expression predicts clinical outcome in breast cancer. Nat Med [Internet]. 2008;14(5):518–27.
22. De Wever O, Mareel M. Role of tissue stroma in cancer cell invasion. J Pathol [Internet]. 2003;200(4):429–47.
23. Azza Rizk, Eman Abdelzaher, Ahmed Gowily RE. Stromal Cd10 expression as a potential novel prognostic factor in invasive breast carcinoma. J R Coll Pathol Aust. 2017;49(1):64–117.
24. Hosni HN, Abd A, Aziz E, Tabak SA, Elsayed M. Immunohistochemical Study of Stromal CD10 Expression in Mammary Duct Carcinoma. Med J Cairo Univ [Internet]. 2012;80(2):37–44.
25. John D, Bancroft MG. Theory and practice of histological techniques. 8th ed. Churchill Livingstone: Elsevier. 2002;125-132.
26. Yamaguchi J, Ohtani H, Nakamura K, Shimokawa I, Kanematsu T. Prognostic impact of marginal adipose tissue invasion in ductal carcinoma of the breast. Am J Clin Pathol. 2008;130(3): 382–8.
27. Van der Vegt B, Wesseling J, Pijnappel RM, Dorrius MD, den Heeten GJ, de Roos M a J, et al. Aggressiveness of true interval invasive ductal carcinomas of the breast in postmenopausal women. Mod Pathol [Internet]. 2010;23(4):629–36.

28. Lu D, Masood S, Khalbuss WE, Bui M. A subset of breast invasive ductal carcinoma with distinctive cytomorphology, aggressive clinical behavior, and unique immunologic profiles. Cancer. 2002;96(5):294–300.

29. Huidrom Jyotsna Devi. A study of CD10 - A stromal marker in breast carcinoma. Acta Scientific Medical Sciences 2.3. 2018; 42-43.

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