

Expression of Stem Cells Marker ALDH1 in Premalignant Lesions, Cancer, Benign Hyperplasia and Normal Duct of Human Breast

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Abstract

Purpose: To study the differences of ALDH1 expression in Invasive Ductal Carcinoma (IDC), Atypical Ductal Hyperplasia (ADH), Usual Ductal Hyperplasia (UDH) and normal ducts and their clinical significance.

Materials and Methods: Immunohistochemistry method was used to detect the expression of ALDH1 in 160 cases of IDC, 50 cases of ADH, 20 cases of UDH and 22 normal duct cases.

Results: ALDH1 was expressed in a few cells in most samples except in a few cases of ADH, UDH and normal ducts, in which ALDH1 expression showed extensive distribution. The positive rate of ALDH1 expression in luminal epithelial cytoplasm of IDC, ADH and UDH was 35%, 64% and 80%, while in myoepithelial cells and stroma of IDC, ADH and UDH was 40%, 52% and 70%. ALDH1 expression in luminal epithelial cytoplasm of IDC has correlation

Aldehyde Dehydrogenase 1 (ALDH1) is a basic substance used in the function and metabolism of the normal stem cells and cancer stem cells. A large number of clinical experiments indicate that breast cancer cells that possess high ALDH1 activity [19] contribute to recurrence and metastasis, leading to poor prognosis and lower survival rates. A series of reports prove that ALDH1 can be used as an ideal marker of breast cancer stem cells [20]. Dong Yi [21] has shown

After inhibiting the endogenous peroxidase activity with 3% H₂O₂, non-specific binding was blocked by incubating the slides with non-immune serum for 15 min, then by incubating the sections with the primary antibody at 4°C overnight. Next, the sections were incubated with a secondary antibody for each marker at 37°C for 15 min, then with the avidin-biotin-peroxidase complex solution at 37°C for 15 min. The antigen-antibody reaction was visualized with DAB at room temperature without light for 5 min and counterstained with hematoxylin.

Two previous studies [20,25-27] have shown that the ALDH1

	ALDH1 positive expression	ALDH1 negative expression	Expression rate	2	P
IDC	64	96	0.4	7.65	0.022
ADH	26	24	0.52		
UDH	14	6	0.7		

first reported human malignant tumor stem cells in people with CD34⁺CD38⁻ phenotype of acute myelogenous leukemia stem cells.

for only 2% of the cancer cells in the mice, but this small number of cells has unlimited self-renewal and malignant differentiation ability, thus making ALDH1 one of the ideal markers of breast cancer stem cells.

According to the results of our study, the positive expression rate of ALDH1 in the cytoplasm of IDC, ADH and UDH was 35%, 64% and 80%, while in the stroma of IDC, ADH and UDH, the expression rates were 40%, 52% and 70%, respectively. We also detected ALDH1 expression in myoepithelial cells and observed that ALDH1 positive stem cells in the mammary gland had properties of basal-like cells [32]. The expression of ALDH1 in the cytoplasm of IDC has a correlation with the OS and RFS of the breast cancer patients ($P < 0.05$), but the expression of ALDH1 in the stroma of IDC has no correlation with the OS and RFS of the breast cancer patients ($P > 0.05$). This differs from the study of Bednarz-Knoll [22]. Dr. Schwartz et al. [33] reported ALDH1 expression was higher in stroma components of benign compared with cancerous lesions, but in our study the difference of ALDH1 expression in the stroma of three kinds of tissues has no statistical significance.

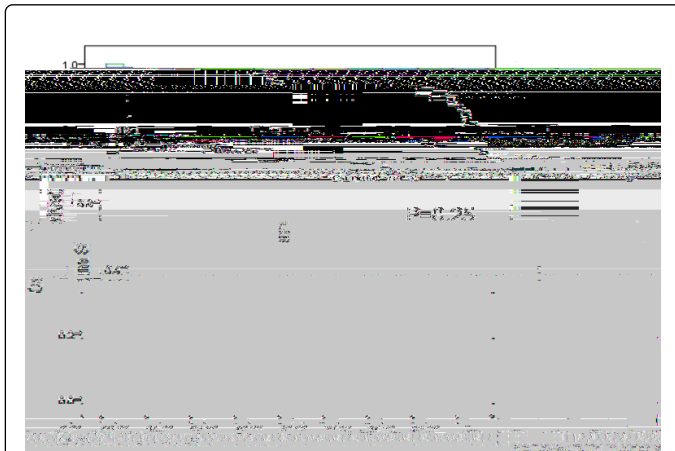


Figure 6 Relapse-free survival. Kaplan-Meier relapse-free survival plots of patients with negative ALDH1 expression (+), positive ALDH1 expression in the stroma of IDC (+).

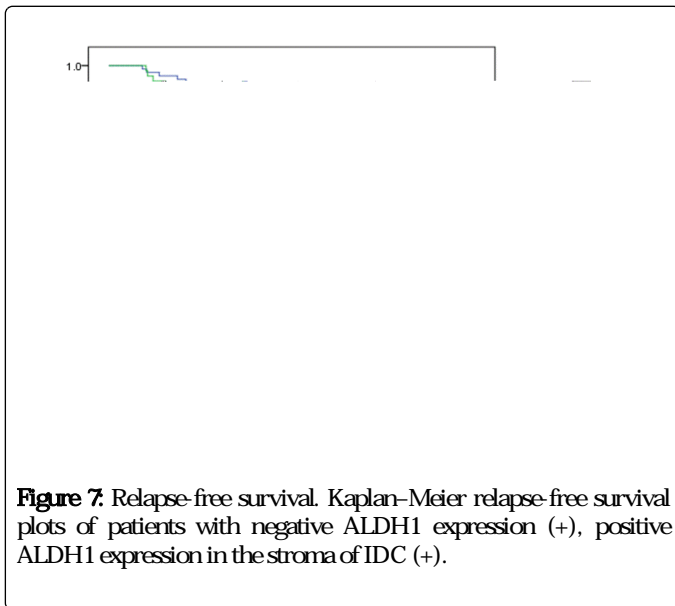


Figure 7 Relapse-free survival. Kaplan-Meier relapse-free survival plots of patients with negative ALDH1 expression (+), positive ALDH1 expression in the stroma of IDC (+).

Then, a large number of studies found tumor stem cells in a variety of malignant tumors. Cancer stem cells, which occupy about 2% of the tumor cells, are insensitive to all sorts of auxiliary treatments; this can lead to the recurrence and metastasis of breast cancer. Therefore, marking the small number of cancer stem cells, finding the corresponding target, and matching the target therapy for a malignant tumor is very important for an effective, radical cure. Breast cancer stem cells are similar to breast epithelial stem cells; however, they also have unlimited proliferation and malignant differentiation ability, which is linked to the growth, recurrence, and metastasis of a tumor. In 2007, Balicki [31] used ALDH1 to identify and isolate breast cancer stem cells, which suggested that ALDH1 may be an ideal and reliable marker for breast cancer stem cells. At the same time, Ginestier et al. [19] found that there only 500 ALDH1 positive cells were needed to develop the cells of Nonobese Diabetic/Severe Combined Immunodeficiency (NOD/SCID) mice into a tumor. This is accounted

