

Stem cell : New Implication for Target Therapy and Prognosis Marker for Breast Cancer

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ABSTRACT

The breast cancer stem cells hypothesis is a new paradigm which has major impact on the treatment by suggesting a new target for cancer therapy. Failure of the long term clinical remission, by advance hormonal receptor therapy, targeting cancer stem cell would be the powerful way to beat cancer in future. Currently <5 cancer stem cells in 7.5 ml blood is used as prognostic marker in metastatic and recurrent breast cancer. CD44+ / CD24- or low phenotype have been identified to the key cell surface marker of promising target. Thus future therapy will need to effectively target the breast cancer stem cell (BCSC) to induce clinically significant remission of diseases.

Key words: Stem cell, BCSC, CD44+, Prognostic marker, Target therapy, Immunophenotype.

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death among females.¹ The concept of cancer stem cells responsible for tumor origin, maintenance and resistance to treatment has gained prominence in the field of breast cancer research.² Presently breast cancer patient have been treated with effectively hormone receptor target therapy depending on ER, PR, HER2 status.³ Targeting cancer stem cells could be powerful way to beat cancer in future. The hypothesis that tumor may originate from a rare population cancer stem cells has gained tremendous popularity in recent year and is supported extensively by several pioneering works.⁴ The therapeutic target of this cell has the potential to eliminate residual disease and may become an important component of a multi modality treatment.

In contrast to the cancer cells, cancer stem cells are slow dividing and have a lower ability to undergo apoptosis and high ability to DNA repair, making them more resistant to traditional method of cancer treatment such as radiation and chemotherapy.⁵ Thus traditional cancer therapy is effective to some tumors but often fail to produce long term clinical remission.

Recent improvement in immunotherapy leading to target of tumor associated antigen has advanced the prospect of targeting breast cancer stem cell (BCSC).^{2,6} Identification of key cell surface marker on stem cells is there mandatory to achieve improved therapy. This is defined the prognostic value of cancer stem cell marker in metastatic and recurrent breast cancer. Currently <5 cancer stem cells in 7.5 ml blood is used as prognostic marker for follow-up to predict chemo response in breast cancer.⁷

The invasive and mesenchymal property of Breast cancer cells with a CD44+/CD24- or low phenotype have been suggested to made them a promising target for eliminating the metastatic capacity of primary tumor.^{7,8} CD44+/CD24- or low phenotype have more tumor initiating properties with stem cell like and invasive feature, though it is unclear their clinical implication.⁹

In vitro experiments, using cell line culture have shown that BCSC with CD44+/CD24- or low resemble the cell type in breast cancer. This cell is capable of diseases recurrence and resistant to chemotherapy and radiation.¹⁰ These cells also retain the ability of self renewal and differentiation capacity. It is reported that Human Breast cancer stem cell (BCSC) identified on basis of CD44+/CD24- or low Lin- expression, could form tumor in non obese diabetic mice.¹¹ It is also reported that population of CD44+/CD24- or low human breast cancer cells were enriched tumorigenic potential¹²

The breast cancer stem cells hypothesis is a new paradigm that could have major impact on the treatment of diseases by suggesting a new target for cancer therapy. Transformed mammary cells have been identified as a potential source of breast cancer, tumor relapse and tumor metastasis.¹³ Current treatment of cancer have shown efficiency and efficacy in removing the bulk of differentiated cancer cells while failing to eliminate cancer stem cells responsible to tumor relapse.³ Thus future therapy will need to effectively target the breast cancer stem cell (BCSC) to induce clinically significant remission of diseases. Identification of target antigen for BCSC need to be further defined so that effective targeting can realize and disrupt cancer stem cells niche and spare normal stem cells niche.

More ever observing, analysis and correlating the changes in expression of cell surface marker of BCSC in breast cancer patient would serve a better way to monitor

patient clinical condition with drugs. This approach might lead to more meaningful clinical remission. Hence the ability to therapeutically attack stem cells hinge upon identifying unique target like cell surface marker.

Hormonal receptor target therapy³ and screening of BRCA1 and BRCA2 genes^{14,15} is not enough for treatment as well as prognosis value for event free survival in breast cancer, rather identification of Breast cancer stem cell (BCSC) from breast tissue shows the better implication for targeting therapy to reduce chance of relapse.

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