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HER2 Dynamics: Advances in Breast Cancer Treatment

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Abstract: Breast cancer is one of the most deadly diseases all over the world. Recent findings suggest that $HER2^+$ and $HER2^-$ Circulating Tumour Cells (CTCs) of metastatic breast cancer interconvert spontaneously and combined treatment with paclitaxel and Notch inhibitors achieves sustained suppression of tumorigenesis implicating novel therapeutic strategy to treat this devastating disease.

Keywords: HER2, Breast Cancer, Circulating Tumour Cells (CTCs)

1. Introduction

Breast cancer is the second most common cancer worldwide, and the leading cause of cancer death in women. Metastatic breast cancer is defined as the spread of cancer cells from breast and regional lymph nodes to other organs of the body. Metastatic breast cancer can be classified into four subgroups [1-4]; (i) Luminal A (HR+/HER2-): This type of breast cancer expresses the estrogen receptor (ER+) and/or the progesterone receptor (PR+) but not HER2 (HER2-), (ii) Luminal B (HR+/HER2-/+): This type of breast cancer expresses ER+ and/or PR+ and is further defined by being highly positive for Ki67 (indicator of proliferating cells) or HER2, (iii) HER2-enriched (HR-/HER2+): This type of breast cancer expresses high level of HER2 and does not express hormone receptors, (iv) Triple negative (HR-/PR-/HER2-): This type of breast cancer does not express ER-, PR-, and HER2-. This is more common in premenopausal women and those with a BRCA1gene mutation.

Drug resistance is a major obstacle in metastatic breast cancer treatment [5-11]. In advanced oestrogen-receptor (ER)-positive/human epidermal growth factor receptor 2 (HER2)-negative breast cancer, circulating tumour cells (CTCs) acquire a HER2-positive subpopulation after multiple courses of therapy [12, 13].

2. Results

Recently, Jordan, N. V. *et al.* described that most of circulating tumour cells (CTCs) expressing HER2 in $ER^+/HER2^-$ breast cancer [14]. The authors found that $HER2^+$ and $HER2^-$ CTCs interconvert spontaneously, and oxidative stress or cytotoxic chemotherapy enhances transition from $HER2^+$ to the $HER2^-$ phenotype. Interestingly, $HER2^+$ CTCs are more proliferative but not addicted to HER2, and $HER2^-$ CTCs demonstrate reduced chemosensitivity but have enhanced sensitivity to Notch inhibition. Combined treatment with paclitaxel and Notch inhibitors achieves sustained suppression of tumorigenesis in orthotopic circulating tumour cell-derived tumour models.

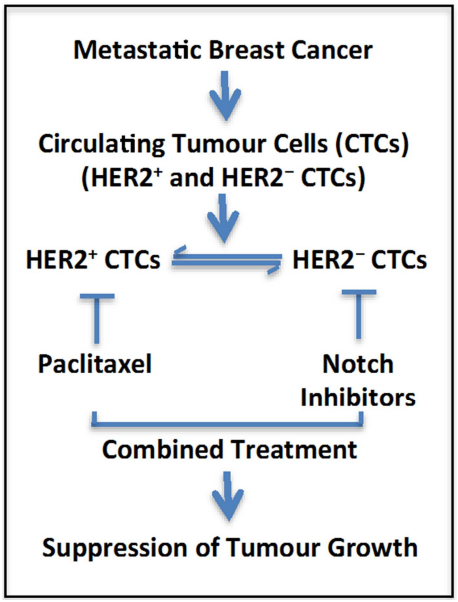

Figure 1. *HER2 Dynamics is involved in Breast Cancer Treatment.*

Figure 1. Schematic diagram of model shows Circulating Tumour Cells ($HER2^+$ and $HER2^-$ CTCs) can interconvert spontaneously, and combined treatment with paclitaxel and Notch inhibitors achieves sustained suppression of tumorigenesis. Courtesy of Jordan, N. V. *et al.* (modified by M. K. Hasan).

3. Conclusion

Taken together, these results suggesting new therapeutic strategy to treat metastatic breast cancer that showed resistance to drug therapy.

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