International Journal of Innovative Research in Medical Science (IJIRMS)
Volume 09, Issue 09, September 2024,
https://doi.org/10.23958/ijirms/vol09-i09/1947

Mini Review

Recent Progress of Pre-targeting Methods in the Fight Against Breast Cancer

Zhi-Gang Sun *[1], Yu-Cui Song [3], Zhi-Na Li [2], Zhi-Guo Zhang [2]

[1]Central Laboratory, Linyi Central Hospital, No.17 Jiankang Road, Linyi 276400, China.
[2]Department of Imaging, Linyi Central Hospital, No.17 Jiankang Road, Linyi 276400, China.
[3]Operating Room, Linyi Central Hospital, No.17 Jiankang Road, Linyi 276400, China.

*Corresponding author: Zhi-Gang Sun; *zhigangsunny@163.com*

Received 02 August 2024; Accepted 04 September 2024; Published 10 September 2024

Abstract

Breast cancer is a malignant tumor that seriously affects women's physical and mental health. Drug resistance and side effects pose challenges to targeted treatment of breast cancer. In recent years, there have been many studies on pre-targeting technology in the treatment of various diseases. This article reviews the recent research progress of pre-targeting technology in the fight against breast cancer.

Keywords: ***breast cancer, progress, method, pre-target, barnase.***

Introduction

Breast cancer is a major disease affecting human health. The incidence of breast cancer in the world increased 1.28 times from 1990 to 2019 [1]. The number of new cases of breast cancer exceeded 2.3 million, and the number of deaths exceeded 685000 in 2020. By 2040, due to aging and population growth, the burden of breast cancer is expected to increase to more than 1 million deaths and 3 million new cases every year [2]. In addition to strengthening the monitoring of female breast cancer, more attention should be paid to men who have bad habits such as smoking and drinking alcohol.

At present, the main treatment strategies for breast cancer include radiotherapy, surgery, targeted therapy, chemotherapy and immunotherapy. Although the specificity for cancer cells has been improved, cancer patients receiving targeted therapy may experience various side effects and toxicity [3]. Radioimmunotherapy has exhibited promising results in hematological malignancies, which also showed high radiation toxicity. The key to pre-targeting is the concept of separating the targeted carrier from cytotoxic drugs and administering them separately. This method can improve the therapeutic index, as it could reduce the side effects caused by off-target toxicity, thereby increasing efficacy due to higher tolerated doses [4]. This article focuses on the application of pre-targeting technology in the breast cancer treatment in recent years.

Pre-targeting Methods in breast cancer treatment

AvidinOX, an avidin variant, was found to have the ability to bind interstitial and cellular protein amino groups via Schiff's base with a tissue half-life of 2 weeks. Data showed that AvidinOX could efficiently capture 90Y-biotinDOTA after administered intranipple in the transgenic BALB/neuT mice, which can eradicate multifocal cancer lesions [5].

HER2/neu-negative BT-20 and -positive BT-474 human breast cancer cell lines were pre-targeted with BAAC and then targeted with multi-Dox loaded PGA modified with DTPA (D-Dox-PGA). When BT-20 or BT-474 cells was pre-targeted with BAAC and then targeted with D-Dox-PGA, enhanced tumor cell killing rate was observed in BT-474 cells. Pre-targeting with BAAC exhibited more tumor cell death in BT-474 cells due to targeted delivery of D-Dox-PGA compared to cancer cells treated with D-Dox-PGA without pre-targeting [6].

Selin Seda Timur et al. combined an anticancer peptide, LyP-1, with a monoclonal anti-DTPA antibody to obtain more selective targeting compound through the p32 receptor and the capture of drug-loaded-polymers. Moreover, targeted Dox-LyP-1 conjugates showed larger tumor toxicity than that of free doxorubicin hydrochloride, whereas non-targeted polymer-drug conjugates showed non-toxic to malignant cells [7].

Sarah M Cheal et al. demonstrated that DOTA-PRIT could be successfully adapted to the internalizing antigen-antibody system with sufficient therapeutic indice and absorbed tumor doses to possess a high probability of curing established human breast cancer xenografts while sparing critical organs with significant radiotoxicity [8].

Wenchao Gu et al. performed 3-step PRIT utilizing the sequential injection of (1) biotinylated bevacizumab, (2) avidin, and (3) radiolabeled StAv to treat triple-negative breast cancer (TNBC). This method achieved low kidney uptake and fast blood clearance, and showed a certain degree of therapeutic effect [9].

Nannan Zhang et al. utilized a liposome-based pre-targeted system modified with targeting peptide CREKA and single-stranded DNA for multimodality imaging-guided pre-targeted synergistic therapy of metastatic breast cancer [10].

PLGA nanocapsules modified with Nile Blue and doxorubicin were used for 2-step targeted delivery via the barnase/barstar protein “bacterial superglue”. 2-step delivery

displayed more effective than one-step delivery in both imaging and tumor therapy [11].

Conclusions

Breast cancer still poses a threat to the health of individuals, and traditional treatment methods cannot completely defeat breast cancer. Pre-targeting technology, as an alternative weapon, has already been used for cancer diagnosis and treatment. The strategy of pre-targeted therapy for breast cancer is mainly based on biorthogonal click, avidin/biotin and other specific reactions. The pre-targeting strategy is an effective supplement to the targeting strategy, and it is expected that the pre-targeting weapons for breast cancer can be developed in the future.

List of abbreviations

BAAC: Bispecific affibody–antibody complex
Dox: Doxorubicin
PGA: Polyglutamic acid
DTPA: Diethylene triamine pentaacetic acid

Funding Statement

This article was funded by the Science and technology development plan project of Shandong Society of Geriatrics (NO. LKJGG2021W074).

References

[1] Xu, Y.; Gong, M.; Wang, Y.; Yang, Y.; Liu, S.; Zeng, Q., Global trends and forecasts of breast cancer incidence and deaths. *Scientific Data* 2023, 10 (1), 334.

[2] Arnold, M.; Morgan, E.; Rumgay, H.; Mafra, A.; Singh, D.; Laversanne, M.; Vignat, J.; Gralow, J. R.; Cardoso, F.; Siesling, S.; Soerjomataram, I., Current and future burden of breast cancer: Global statistics for 2020 and 2040. *The Breast* 2022, 66, 15-23.

[3] Min, H.-Y.; Lee, H.-Y., Molecular targeted therapy for anticancer treatment. *Experimental & Molecular Medicine* 2022, 54 (10), 1670-1694.

[4] Verhoeven, M.; Seimbille, Y.; Dalm, S. U., Therapeutic Applications of Pretargeting. *Pharmaceutics* 2019, 11 (9), 434.

[5] De Santis, R.; Leoni, B.; Rosi, A.; Albertoni, C.; Forni, G.; Cojoca, R.; Iezzi, M.; Musiani, P.; Paganelli, G.; Chinol, M.; Carminati, P., AvidinOX™ for Highly Efficient Tissue-Pretargeted Radionuclide Therapy. *Cancer Biotherapy and Radiopharmaceuticals* 2010, 25 (2), 143-148.

[6] Gada, K. S.; Patil, V.; Panwar, R.; Hatefi, A.; Khaw, B. A., Bispecific antibody complex pre-targeted delivery of polymer–drug conjugates for cancer therapy. *Drug Delivery and Translational Research* 2012.

[7] Timur, S. S.; Bhattarai, P.; Gürsoy, R. N.; Vural, İ.; Khaw, B.-A., Design and In Vitro Evaluation of Bispecific Complexes and Drug Conjugates of Anticancer Peptide, LyP-1 in Human Breast Cancer. *Pharmaceutical Research* 2017, 34 (2), 352-364.

[8] Cheal, S. M.; Xu, H.; Guo, H. F.; Patel, M.; Cheung, N. K. V., Theranostic pretargeted radioimmunotherapy of internalizing solid tumor antigens in human tumor xenografts in mice: Curative treatment of HER2-positive breast carcinoma. *Theranostics* 2018, 8 (18), 5106-5125.

[9] Gu, W.; Yudistiro, R.; Hanaoka, H.; Katsumata, N.; Tsushima, Y., Potential of three-step pretargeting radioimmunotherapy using biotinylated bevacizumab and succinylated streptavidin in triple-negative breast cancer xenograft. *Annals of Nuclear Medicine* 2021, 35 (4), 514-522.

[10] Zhang, N.; Shu, G.; Qiao, E.; Xu, X.; Shen, L.; Lu, C.; Chen, W.; Fang, S.; Yang, Y.; Song, J., DNA-functionalized liposomes in vivo fusion for NIR-II/MRI guided pretargeted ferroptosis therapy of metastatic breast cancer. *ACS Applied Materials & Interfaces* 2022, 14 (18), 20603-20615.

[11] Shipunova, V. O.; Komedchikova, E. N.; Kotelnikova, P. A.; Nikitin, M. P.; Deyev, S. M., Targeted Two-Step Delivery of Oncotheranostic Nano-PLGA for HER2-Positive Tumor Imaging and Therapy In Vivo: Improved Effectiveness Compared to One-Step Strategy. *Pharmaceutics* 2023, 15 (3), 833.