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Co-Delivery of Zirconium-89 and Photosensitizer by CXCR4-Positive Cell Membrane Nanocarriers for PET Diagnosis and Phototherapy on Breast Cancer

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Extended Abstract

Background:

Malignant tumor is one of the major diseases threatening human health. Radionuclide has been used in cancer diagnosis and treatment because of its advantages. However, due to the lack of specificity on target site, the normal organ toxicity hinders further clinical application of radionuclide and therapeutic drug. Nanosized drug delivery systems have achieved enormous improvements in targeted therapeutics. Cellular membrane nanovesicles (MNVs) offer the advantage of being able to fully replicate the diversity of antigens on the surface source cells for precise targeting[1,2]. However, the mechanism regarding the homotypic affinity of cancer cells remains unclear.

Methods:

Mass spectrometry and RNA sequencing were used to explore the mechanism regarding the homologous targeting of cancer cell derived MNVs (CC-MNVs). The adhesive proteins and chemokines between the MDA-MB-468 and MDA-MB-231 breast tumors were compared, and the corresponding antagonists were administrated *in vivo*. After blocking, CC-MNVs was injected intravenously on tumor models for imaging by IVIS Spectrum. Radionuclide ^{89}Zr was coupled with free amino group on cell membrane nanovesicles using bifunctional chelating agent p-NCS-Bz-DFO for PET diagnosis. NIR photosensitizer IR780 was loaded into CC-MNVs for photothermal therapy.

Results:

In vivo imaging showed that MNVs from MDA-MB-468 cells (M468-MNVs) can actively recognize the homologous MDA-MB-468 breast tumor but “bypassing” the coexisting heterologous MDA-MB-231 breast tumor. The secreted chemokine from two kinds of tumor tissues were detected and the results showed that many kinds of chemokine were high secreted in MDA-MB-468 tumors (e.g. CXCL12, CCL19), not in MDA-MB-231 tumors. After blocking of CXCR4/CXCL12 or CCR6/CCL19 axis pathway, M468-MNVs showed lower fluorescence signal in MDA-MB-468 tumor tissues. Furthermore, the fluorescence of shCXCR4-MNVs decreased significantly in M468 tumors, compared with that of shNC-MNVs. After high efficiency of targeting into tumor tissues, CXCR4-positive M468-MNVs were applied to deliver radionuclide and photosensitizer IR780. 89Zr-coupled M468-MNVs displayed excellent accumulation in MDA-MB-468 tumor region from 6 h to 48 h post-injection. Upon laser irradiation, the tumor volume in CXCR4-positive M468-MNVs treatment group was significantly reduced. In addition, major organs of CXCR4-positive M468-MNVs treatment group showed unnoticeable pathological changes, suggesting the negligible organ damage and low toxicity of M468-MNVs.

Conclusion:

In summary, the CXCR4-positive CC-MNVs platform have great advantages with outstanding antitumor efficiency and safety on tumor models with highly secreted CXCL12.

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