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Combination of photothermal, prodrug and tumor cell camouflage technologies for triple-negative breast cancer treatment

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Traditional medicine has been widely uTriple-Negative Breast Cancer (TNBC) remains the most challenging breast cancer subtype. In the presented work, we have combined several emerging technologies to build up a nanoplatform for TNBC treatment: photothermal therapy, prodrug design and tumor cell camouflage formulation. First, we synthesized a paclitaxel (PTX) based prodrug PTX-SS, and then conjugated it to the surface of gold nanorod (Au NR) @ mesoporous silica (MSN) core-shell nanoparticles (Au@MSN-NH2 NPs). Subsequently, doxorubicin (DOX) was loaded into the Au@PTXSS-MSN NPs and further coated with cell membranes isolated from MDA-MB-231 cells to form cell camouflaged Au@PTXSS-MSN/DOX@CM NPs. The Au@PTXSS-MSN/DOX@CM NPs exhibited very good DOX loading capacity and the prodrug strategy enabled the precise adjustability of PTX-SS loading to achieve the optimized ratio between PTX and DOX to maximize the synergistic effect of these two drugs, as well as enabled GSH-responsive intracellular drug release. More interestingly, the cell membrane coating not only protected the drug from premature release, but also significantly improved the targeting ability of NPs to breast cancer MDA-MB-231 cells. The NPs also showed good photothermal responsiveness with clear improvement in inhibiting MDA-MB-231 cell proliferation under laser irradiation. The in vivo studies further confirmed the effectiveness of Au@PTXSS-MSN/DOX@CM NPs on TNBC tumor inhibition in 4T1 cell grafted tumor mice model.

Importance of Research: Triple-Negative Breast Cancer (TNBC) is the most aggressive breast cancer that is accompanied by poor prognosis and high rate of recurrence and metastasis. The using of targeted anti-cancer drugs (such as Herceptin, Lapatinib and Pertuzumab) has dramatically improved the prognosis of breast cancer; however, TNBC still lacks effective therapeutic drugs due to the lack expression of hormone receptors (include estrogen receptor, progesterone receptor and human epidermal growth factor receptor 2), which are widely used for breast cancer targeting therapy. Cell camouflage technologies that utilize cancer cell originating cell membranes to hidden the drug carrier nanoparticles (NPs), have been found to be a good strategy for targeted cancer therapy owing to the extensive homology of the proteins and antigens between the cell membrane and cancer cells, as well as the homing ability of cancer cells. In summary, we have developed a new photothermal and GSH responsive NP with cell camouflage for targeted TNBC therapy. The Au NRs were embedded into the Au@PTXSS-MSN/DOX@CM with photothermal therapy activity, while the porous shell structure formed by MSN realized the high drug loading capacity to load the hydrophilic DOX. The prodrug technology enabled the PTX prodrug to have a GSH responsive linker and a conjugation site for conjugating onto the MSN. The coated cell membrane originating from tumor cells can protect the drugs from premature releasing and greatly improved the tumor targeting efficiency. Au@PTXSS-MSN/DOX@CM NPs have been

confirmed to have good tumor cell targeting and synergistic anti-tumor effects at the cellular level. In addition, the Au@PTXSS-MSN/DOX@CM NPs also generated significant anti-tumor activity in vivo, as well as further improve the on-site drug release, for targeted TNBC therapy.

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Biography

Xiaodong Ma began to study for a PhD at Abo Akademi University in 2020. His research includes functional biological nanomaterials, with an emphasis on prodrug synthesis, nanocarrier synthesis and related biological applications. During his research, Dr. Ma constructed several nano drug delivery vehicles based on stimulation-responsive mesoporous silicon dioxide nanoparticles (MSNs) and prodrug nanoparticles. By utilizing the stimulation characteristics of tumor microenvironment and external light source, Dr. Ma realized the controlled release of antitumor drugs, immunosuppressants and bioactive macromolecules to enhance the tumor treatment effect, paving the way for the application of prodrugs in the biomedical field.

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