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The Accumulation of Upconverting Nanoparticles in Different Subtypes of Breast Cancer Cells

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Extended Abstract

Breast cancer is the second leading cause of cancer-related death in women worldwide. Although breast cancer screening programs leads to the early detection of the cancer disease, late stage metastatic breast cancer is still hard to control and completely eradicate. Significant differences in individual tumors suggest that tumor cells are heterogenous and possess various phenotypes with diverse functions and expression of different markers. Basal-like breast cancer subtype is considered to be one of the most aggressive ones and it is known as triple-negative breast cancer (TNBC). Currently, there is no molecular-based targeted therapy for aggressive subtype TNBC. Therefore, TNBC is one of the highest priorities of current breast cancer research [1].

Upconverting nanoparticles (UCNPs) hold the potential for biomedical application. UCNPs absorb and convert near-infrared (NIR) light into visible (Vis) and ultraviolet (UV) radiation. NIR excitation offers a possibility to penetrate deeper into biological tissues due to "biological NIR window". The emitted UV-Vis and NIR photons can be used for cancer treatment and imaging, respectively, thus enabling to perform both functions in one agent – diagnostics and therapy (Theranostics). Synthesis procedure of UCNPs involves organic solvents, therefore UCNP carry hydrophobic oleate groups on surface, which makes them unstable in aqueous solutions and non-biocompatible. Coating with amphiphilic polymers or phospholipids is an effective way to hydrophilizing UCNPs surface, which can also form functional groups capable of attaching various biomolecules [2].

The goal of our study was to select the most biocompatible UCNPs and label the aggressive phenotype of breast cancer. In order to distinguish the aggressive subtype of breast cancer, the expression of surface markers, clonogenic assay and chemoresistance was investigated. We chose MDA-MB-231 and MCF-7 breast cancer cells and performed all the above mentioned tests. For the UCNPs accumulation studies we used LiYF4:Tm3+,Yb3+ upconverting nanoparticles (UCNPs) [3], functionalized by p(MAA-co-PEG9MEMA) polymers. The polymers used for surface modification differed in the density of PEGylated substituents (PEG-25 and PEG-75). Finally, we looked at how these coatings affect the colloidal stability of UCNPs in biological media, and intracellular uptake into different subtypes of human breast cancer cells.

The flow cytometry results revealed that 100% of MDA-MB-231 cells expressed CD44 marker while the expression of CD24 was very low (~2%). In contrast to MDA-MB-231, MCF-7 cells exhibited high expression of CD24 (94%) and low expression of CD44 (11 %). EpCAM was expressed in both cell lines. The high expression of CD44 and low expression of CD24 is associated with stem-like aggressive properties [4]. Colony formation efficiency was 2 times higher in MDA-MB-231 cells, as well as resistance to chemotherapeutic drug doxorubicin. Thus, MDA-MB-231 triple negative breast cancer cells represent the aggressive phenotype of breast cancer cells. Laser scanning confocal microscopy revealed that the best cellular uptake (evaluated from the UCNPs emission intensity) for both cell lines is observed for PEG-25 modified UCNPs. This result is rather unexpected, since PEG-75 modified UCNPs are more stable in both DMEM and DMEM+FBS, whereas PEG-25 modified UCNPs are sufficiently stable only in DMEM+FBS. If we compare the UCNPs accumulation rate between MDA-MB-231 and MCF-7 cells, emission intensity was almost the same for both MDA-MB-231 and MCF-7 cells and did not depend on PEGylated substituents.

In conclusion, $LiYF_4:Tm^{3+},Yb^{3+}$ UCNPs modified with PEG_9MEMA-25 was the most biocompatible and accumulated similarly in both phenotypes of breast cancer cells, therefore can be considered as a suitable candidate for future development of targeted therapy against aggressive subtypes of breast cancer.

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