Peptide Modified Polymeric Micelles Specific for Breast Cancer Cells

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Abstract:

The specific targeting ability of novel breast cancer targeting peptides as ligands coupled to polymeric micelles was evaluated in the present study. In this context, engineered breast cancer cell targeting peptides, denoted as peptide 11 (RGDPAYQGRFL) and peptide 18 (WXEAAYQRFL), were compared with the lead 12-mer p160 peptide and cyclic RGDfK peptide. All four peptides were conjugated individually to poly(ethylene oxide)-b-poly(caprolactone) (PEO-b-PCL) diblock polymeric micelles to obtain targeted carrier systems PM11, PM18, PM 160, and PM c-RGD. Physical blending of the peptides 11 and 18 with PEO-b-PCL was also done to yield combination micelles, comPM11 and comPM18. The structural confirmation of polymer was carried out using 1H NMR and MALDI-TOF, and the size distribution and zeta potential of the micelles were determined using dynamic light scattering. Lipophilic cyanine fluorescent probe DiI was physically incorporated in the polymeric micelles to imitate the hydrophobic drug loaded in the micellar core. The cellular uptake of DiI-loaded peptide-containing polymeric micelles by MDA-MB-435, MDA-MB-231, and MCF7 breast cancer cell lines, as well as HUVEC and MCF10A noncancerous cells, were analyzed using flow cytometry and confocal microscopy techniques. Modification of polymeric micelles with peptide 11 or 18 led to an increase in micellar uptake specifically in breast cancer cells compared to p160, c-RGD modified, or naked micelles. The peptide−micelle combinations (comPM11 and comPM18) displayed better uptake by the cells compared to the covalently conjugated PM11 and PM18 micelles; however, the combinations were less selective toward cancer cells. The results point to a potential for peptides 11- and 18-micelle conjugates as attractive platforms for improved performance of a wide range of chemotherapeutic drugs and/or imaging agents in cancer therapy and diagnosis.

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