

Abstract Submitted
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Targeting cancer cell invasiveness using homing peptide-nanocomplexes GIULIA SUARATO, Materials Science and Engineering, Stony Brook University, JILLIAN CATHCART, Molecular and Cellular Pharmacology, Stony Brook University, WEIYI LI, Materials Science and Engineering, Stony Brook University, JIAN CAO, Medicine, Cancer Prevention, Stony Brook University, YIZHI MENG, Materials Science and Engineering, Stony Brook University — Matrix metalloproteinase-14 (MMP-14) plays critical roles in digesting the basement membrane and extracellular matrix and inducing cancer migration. We recently unraveled a unique role in cell invasion of the hemopexin (PEX) domain of MMP-14. The minimal motif located at the outmost strand of the fourth blade of the PEX domain was identified to form homodimers of MMP-14. A peptide (IVS4) mimicking the binding motif was shown to interrupt MMP-14 dimerization and decrease MMP-14-mediated functions. Since most invasive cancer cells express upregulated MMP-14 at the surface, IVS4 could be used as a cancer homing peptide to specifically deliver cytotoxic drugs for cancer therapy. We developed cancer homing nanocarriers by linking IVS4 to polysaccharide-based micellar nanoparticles (NPs). To determine if conjugation of IVS4 to NPs maintains the IVS4 inhibition of MMP-14 function, substrate degradation and cell migration assays were performed. IVS4-NPs efficiently prevented MMP-14-mediated substrate degradation and cell migration, and were minimally uptaken by non-cancer cells. Importantly, IVS4 confers an uptake advantage compared to the control peptide in MMP-14-expressing cells. Taken together, our findings demonstrate the potential use of IVS4-NPs as novel cancer nanotherapeutics.

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