Non-invasive imaging holds great promise for the early detection and treatment of human disease. The use of “smart” nanoparticles, that combine multiple functions of targeting, imaging and drug delivery, have tremendous potential to increase the sensitivity and specificity of therapies. We investigate the targeting potential of mouse polyomavirus based virus-like particles (VLPs) as vectors for directed cell/tissue delivery of therapeutic or diagnostic compounds. Mouse polyomavirus, type species of Polyomaviridae family, is superior for this kind of research to its human counterparts due to the absence of pre-existing immunity in human population. We intend to target the VLPs to cancer cells by changing the receptor binding site on the major capsid protein VP1. There are four predominant surface-exposed loops (BC, DE, EF and HI) in the VP1 structure, but only BC and HI outfacing loops are responsible for the attachment to the native sialic acid-containing receptor. We selected the BC loop as a candidate site for manipulation and prostate cancer cells as a model system. We used site-directed mutagenesis for insertion of a peptide ligand, which binds to prostate-specific membrane antigen (PSMA). This antigen is overexpressed in androgen-resistant human prostate cancer cells. We investigate the binding specificity of VLPs to PSMA protein in in vitro and in vivo assays. We found the discrepancy between their binding properties and internalization efficiency. The relevancy of these experiments to cell specific targeting and nanoparticle uptake will be discussed.

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