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Noncovalent Antibody-Nanomaterial Conjugates: A Simple Approach to Produce Targeted Nanomedicines

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Abstract : One promising approach to enhance nanomedicine therapeutic efficacy is to include a targeting agent, such as an antibody, to increase accumulation at the tumor site. However, the application of such targeted nanomedicines remains limited, in part due to difficulties involved with biomolecule conjugation to synthetic nanomaterials. One approach recently developed to overcome this has been to engineer bispecific antibodies (BsAbs) with dual specificity, whereby one portion binds to methoxy polyethyleneglycol (mPEG) epitopes present on synthetic nanomedicines, while the other binds to molecular disease markers of interest. In this way, noncovalent complexes of nanomedicine core, comprising a hyperbranched polymer (HBP) of primarily mPEG, decorated with targeting ligands are able to be produced by simple mixing. Further work in this area has now demonstrated such complexes targeting the breast cancer marker epidermal growth factor receptor (EGFR) to show enhanced binding to tumor cells both in vitro and in vivo. Indeed the enhanced accumulation at the tumor site resulted in improved therapeutic outcomes compared to untargeted nanomedicines and free chemotherapeutics. The current work on these BsAb-HBP conjugates focuses on further probing antibody-nanomaterial interactions and demonstrating broad applicability to a range of cancer types. Herein are reported BsAb-HBP materials targeted towards prostate-specific membrane antigen (PSMA) and study of their behavior in vivo using ^{89}Zr positron emission tomography (PET) in a dual-tumor prostate cancer xenograft model. In this model mice bearing both PSMA+ and PSMA- tumors allow for PET imaging to discriminate between nonspecific and targeted uptake in tumors, and better quantify the increased accumulation following BsAb conjugation. Also examined is the potential for formation of these targeted complexes in situ following injection of individual components? The aim of this approach being to avoid undesirable clearance of proteinaceous complexes upon injection limiting available therapeutic. Ultimately these results demonstrate BsAb functionalized nanomaterials as a powerful and versatile approach for producing targeted nanomedicines for a variety of cancers.

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