Active Targeting of PEGylated Nanomedicines with Bispecific Antibodies for Prostate Cancer Therapy

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Strategies to improve therapeutic efficacy of cancer nanomedicines include optimizing physical parameters of nanoparticles (NP) and priming the tumour microenvironment before administration of NPs. Active targeting, which is the conjugation of tumour specific targeting ligands on the NP surface can be additionally employed to improve therapeutic efficacy of nanomedicines[1]. The rational is that while passive targeting through the Enhance Permeability and Retention (EPR) effect localizes NPs into the tumour interstitium, active targeting should enhance tumour cell uptake of these NPs [2].

This research project employs the use of a Bispecific Antibody (BsAb) for active targeting of PEGylated nanomaterials or nanomedicines for use in prostate cancer therapy. The proposed BsAb constitutes dual targeting specificities for methoxy-PEG on the NP surface and the tumour associated cell surface receptor, glypican 1 (GPC-1). Glypican 1 is a heparan sulphate proteoglycan overexpressed in prostate cancer and in prostate cancer cell lines[3]. The latter BsAb antibody format allows for a facile method of conjugating tumour targeting ligands onto the surface of PEGylated NPs through high affinity antibody-antigen interactions as opposed to the use of chemical conjugation methods [4].

In the current project, a novel high affinity human monoclonal antibody against GPC-1 was generated using phage display panning. Following characterization and validation, the antibody was reformatted into the αPEG-αGPC1 bspecific antibody. The αPEG-αGPC1 BsAb was characterized and used to actively target pegylated nanomaterials to prostate cancer cell lines in vitro. An intensive assessment of targeting and therapeutic properties of targeted nanomaterial or nanomedicines will also be performed in vivo using prostate cancer xenografts in murine models. Upon the successful validation, actively targeted nanomedicines will be assessed further in canine models.

References