Glypican-1 as a novel immunotherapeutic target in prostate cancer

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INTRODUCTION AND OBJECTIVES: New effective therapies for men with prostate cancer are desperately needed. Recently, cancer immunotherapy has emerged as an important new treatment strategy for prostate cancer and for castrate resistant prostate cancer (CRPC). Multiple studies have identified the heparan sulfate proteoglycan-1 Glypican 1 (GPC-1) as being overexpressed in different cancers, and also as being a possible marker of poor prognosis in several solid tumor cancers. GPC-1 has been recently identified as a potential marker for prostate cancer. The MIL-38 monoclonal antibody detects GPC-1 and an IgG1 chimeric version of this antibody has been developed for preclinical studies. Here we sought to examine MIL-38 binding to a panel of prostate cancer cell lines and examine its feasibility as a novel immunotherapeutic agent targeting GPC-1 in prostate cancer.

METHODS:
Expression of GPC-1 in CRPC cell lines was examined by Flow cytometry and Western Blotting using MIL-38 as the detector antibody. The competency of GPC-1 as an immunotherapeutic target was assessed via chimeric MIL-38 induced Antibody Dependent Cell Cytotoxicity (ADCC) using high affinity Natural Killer cells (haNKs) *in vitro.*

RESULTS:
Flow cytometry and Western blot assessments of normal prostatic epithelial cells (*i.e.* RWPE-1) and cells from prostate cancer cell lines (*i.e.* PC-3, 22RV1, DU-145, VCaP, LNCaP, CWR-R1, and LAPC-4) revealed that only cancer cells expressed GPC-1. Enzalutamide resistant cell lines demonstrated higher expression of GPC-1 than their respective parental line. ADCC assays demonstrated enhanced haNK – prostate cancer cell cytotoxicity in the presence of chimeric MIL-38 anti-GPC-1 antibody, while the IgG1 isotype control had no effect.

CONCLUSIONS: GPC-1 protein was expressed by most prostate cancer cell lines, including enhanced expression by enzalutamide resistant cells. Preliminary *in vitro* ADCC assay results revealed the potential utility of GPC-1 as an immunotherapeutic target in prostate cancer.

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