Supplementary Information

Engineering Modular Half-Antibody Conjugated Nanoparticles for Targeting CD44v6-Expressing Cancer Cells

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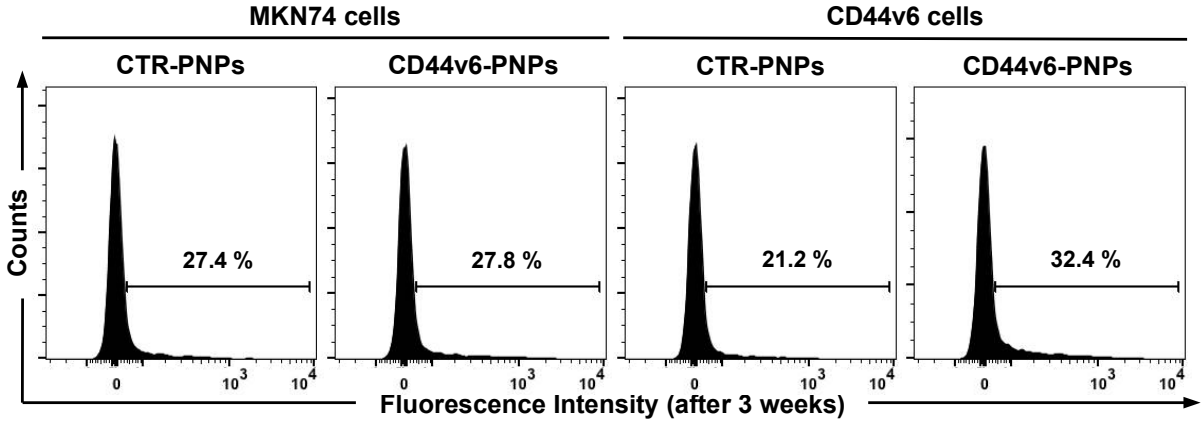

Figure S1. CD44v6 half-antibody conjugated PNPs retain binding to CD44v6 expressing GC cells after storage. Flow cytometry analysis of MKN74 and CD44v6 cell binding to CTR-PNPs and CD44v6-PNPs 3 weeks post-production stored at 4 °C in PBS.

Table S1. Examples of active targeting nanoparticles for cancer therapy. Efficiency of active targeting compared to non-targeted nanoparticles reported in the literature for cancer therapy.

Ligand	Receptor	Nanoparticle	*In vivo*/*in vitro* study	Efficiency compared to non-targeted NPs	Ref
IL-13 peptide	IL-13Rα2	Docetaxel-loaded PEG-PCL	*In vivo*: human primary glioblastoma cell line (U87) orthotopic xenograft	1.73-fold higher tumor targeting	1
CVKTPAQSC peptide	CD133	Docetaxel-loaded PLA	*In vitro:* human lung cancer cell line (A549)	1.88-fold higher cell targeting	2
cRGDyK	Integrin αvβ3	Paclitaxel-loaded micelle	*In vitro:* human prostate cancer cell line (PC-3)	1.93-fold higher cell targeting	3
RGD	Integrin αvβ3	Doxorubicin-dendritic poly-L-lysine-gelatin	*In vivo:* murine mammary carcinoma cell line (4T1) xenograft	1.18-fold higher tumor accumulation	4
Anti-CD44v6 Fab	CD44v6	Bevacizumab-loaded PLGA-PEG	*In vitro:* human stomach adenocarcinoma cell line (MKN74)	2.00-fold higher cell targeting	5
Hyaluronic acid	CD44	Paclitaxel-micelle	*In vivo:* murine hepatic carcinoma cell line (Heps) xenograft	2.80-fold higher tumor accumulation	6
Folic acid	Folate	Doxorubicin-dendrimer	*In vitro:* human epidermal carcinoma cell line (KB)	1.40-fold higher cell targeting	7
Folic acid	Folate	Gemcitabine-loaded BSA	*In vitro:* human breast adenocarcinoma cell line (MCF-7)	2.00-fold higher cell targeting	8
Folic acid	Folate	Doxorubicin-β-cyclodextrin	*In vitro:* human breast adenocarcinoma cell line (MCF-7)	1.98-fold higher cell targeting	9

Aptamer AS1411	Nucleolin	Doxorubicin-loaded HPAEG	*In vitro:* human breast adenocarcinoma cell line (MCF-7)	2.00-fold higher cell targeting	10
Aptamer AS1411	Nucleolin	Methotrexate-UnTHCPSi-PEI	*In vitro:* human breast adenocarcinoma cell line (MDA-MB-231)	1.60-fold higher cell targeting	11
Aptamer AS1411	Nucleolin	Doxorubicin-loaded polymersome	*In vitro:* human breast adenocarcinoma cell line (MCF-7)	1.73-fold higher cell targeting	12
Aptamer AS1411	Nucleolin	Doxorubicin-loaded polymersome	*In vivo:* human breast adenocarcinoma cell line (MCF-7) xenograft	1.75-fold higher cell targeting	12
Galactose	Lecithin	Doxorubicin-loaded solid lipid	*In vitro:* human lung cancer cell line (A549)	1.50-fold higher cell targeting	13
Folic acid and BSA	Folate and SPARC	Paclitaxel-loaded lipid	*In vitro:* human breast adenocarcinoma cell line (MCF-7)	1.90-fold higher cell targeting	14

Abbreviations: BSA – bovine serum albumin; cRGDyK - cyclic arginine-glycine-aspartic acid-tyrosine-lysine; Fab - antigen-binding fragment; HPAEG – hyperbranched poly(2-((2-(acryloyloxy)ethyl)disulfanyl)ethyl 4-cyano-4(((propylthio)carbonothioyl)-thio)-pentanoate-co-poly(ethylene glycol) methacrylate; IL-13 - Interleukin 13; PCL - polyethylene glycol-poly(ε-caprolactone); PEG - polyethylene glycol; PEI - polyethylenimine; PLA - poly(lactic acid); PLGA - poly(lactic-co-glycolic acid); NPs – nanoparticles; RGD - arginine–glycine–aspartic acid peptide; SPARC - secreted protein acidic and rich in cysteine; UnTHCPSi - undecylenic acid modified thermally hydrocarbonized porous silicon.

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