Supplementary Information

Receptor or Rhetoric? A Critical Review of Glucose Transporter-Targeting in Nanomedicine

Short Title: Receptor or Rhetoric: GLUT Targeting in Nanomedicine

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Table S1 Overview of the literature reports reviewed

Ref: reference (same numbering as in the main text).
NP: Nanoparticle type and size.
Linker: chemical nature of linker between glucose moiety and nanoparticle.
Conjugation: indicates site and chemical nature of glucose conjugation; Cx (x=1-6) indicates the carbon of the glucose ring (numbered as shown in Fig. 3 of the main text) at which glucose is conjugated; C(O), carbonyl; N(H), secondary amine; N(suc), N-succinyl.
Uptake meth.: Methodology by which uptake was observed and/or quantified.
GLUT cells: Cell lines with high GLUT expression used for the uptake experiments.
Control cells: Cell lines with low GLUT expression used as control (where appropriate)
Control NPs: Capping layer of non-glycoconjugated NPs used as control (where appropriate)
Glu comp: indicates if glucose competition control experiments were reported.
Inhibitor: indicates if control experiments with GLUT inhibitors or GLUT knock-down methods were reported.

Ref.	NP	Linker	Conjugation	Uptake meth.	GLUT cells	Control cells	Control NPs	Glu comp	Inhibitor
a. Direct attachment of glucose to NP surface									
11	Au (11 nm)	X	C1-S-	ICP-MS	MCF-7	MCF-10A	citrate	X	X
123	Au (~8 nm)	X	C1-S-	ICP-MS	DU-145	X	citrate	X	X
124	Au (11 nm)	X	C1-S-	ICP-MS	DU-145	X	citrate	X	X
125	Au (14 nm)	X	C1-S-	ICP-OES	SK-OV-3	X	citrate	X	X
126	Au (2.6 nm)	X	C1-S-	fluorescence microscopy	U87-MG	SVG p12	glutathione	X	X
127	Au (15 nm)	X	C1-S-	FAAS, TEM	HSG (HeLa)	X	3-mercapto-1-propanesulfonate	X	X
128	Au (20 nm)	X	C1-S-	ICP-MS	THP-1, MCF-7	X	PEG	X	X
129	Ag (61 nm)	X	C2-NH_2-	TEM	Du-145, PC-3	X	citrate/tannic acid	X	X
130	Silica-coated CoFe (~200 nm)	X	C2-N(H)-C(O)-	ICP-OES	MDA-MB-231, MCF-7	MCF-10A	carboxylate	X	X
131	CdTe/CdS QDs (3-7 nm)	X	unspecified	fluorescence microscopy	yeast	X	X	X	X
132	mesoporous silica (200-400 nm)	X	C6(O)-N(H)-	flow cytometry	HeLa, A549	X	aminosilane	X	X

133	MWCNTs	X	C2-N(H)-C(O)-	radiolabelling	MDA-MB-231	X	X	✓	(✓) (negative)
109	Au (2.5 nm)	X	C1-S-	ICP-MS	MDA-MB-231	X	glutathione	(✓) (negative)	✓
b. Short linker between glucose and NP									
135	Ag (80 nm)	4-aminothio-phenol	C1-N(H)-phenyl-S-	FAAS	A549	L929	citrate	X	X
136	Ag (54 nm)	thiopropionic acid	unspecified	ICP-MS, fluorescence microscopy	HepG2, Neuro2a	X	citrate	X	X
137	Fe_3O_4@Au@ PMAO (5 nm)	4-aminophenol	C1-O-phenyl-	fluorescence microscopy	HeLa	X	PEG	X	X
138	iron oxide (6 nm) with PMAO polymer shell	4-aminophenol	C1-O-phenyl-	fluorescence microscopy	Vero	X	PEG	X	X
139	Si (7 nm)	$C_3N(H)C(O)$	C1-C-C(O)-N(H)-	Flow cytometry	SK-MEL-28, A549, MCF-7	MDCK, HHL5	X	X	X
141	Si (4 nm)	$C_2C(O)N(H)C_5$	C1-O-	fluorescence microscopy	HeLa	X	carboxylate	X	X
142	silica (130 nm)	derived from N-(5-Azido-2-nitro-benzoyloxy)-succinimide	C2-N(H)-	ICP-OES	HT1080	X	3-aminopropyl trimethoxysilane	X	X
144	lanthanide NPs (20 nm)	C(O)N(H)CCO	C1-O-	fluorescence microscopy	RAW264.7, MKN-45, HeLa	X	mannose, galactose, fucose, N-acetyl-glucosamine	X	X
145	polyacrylate coated ZnS/CdSe QDs (few nm)	glucose	C1-O-	fluorescence microscopy	HeLa	X	X	X	X
8	CdSe QDs (3-5 nm)	mercapto-succinic acid	C2-N(H)-C(O)-	fluorescence microscopy	X	HEK293T	mercaptosuccinic acid	X	X

146	Ag_2Se QDs (3.6 nm)	glutathione	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	MCF-7, SW1990	X	glutathione	X	X
147	Au (4 nm)	mercapto-succinic acid	C2-N(H)-C(O)-	computed tomography contrast	A549	X	citrate	X	X
148	apoferritin nanocages (12 nm) containing AuNP (4 nm)	aspartic/ glutamic acid	C2-N(H)-C(O)-	ICP-MS	MCF-7	MCF-10A	no ligand	X	X
150	glutenin (200 nm)	amino acid side chains with NH_2	C1-N(H)-	cell viability	MCF-7	X	X	X	X
151	LIPs (100 nm)	octyl (embedded in liposome)	C1-O-	fluorescence microscopy, flow cytometry	HepG2	L02	no ligand	X	X
152	Chitosan (~200 nm)	succinyl	C2-N(suc)-	fluorescence microscopy	4T1	X	no ligand	X	X
153	methacrylate glycol-block copolymer	4-6 bonds	C1-O-	fluorescence microscopy, flow cytometry	MCF-7, MDA-MB-231, A2780	X	galactose, fructose	X	X
154	iron oxide/PEG (30 nm)	C(O)OCC(OH) CS	C1-O-	Prussian blue staining, ICP-OES	A459	X	no ligand, mannose	X	X
155	Au (2nm)	mercapto-ethoxy	unspecified	TEM	hCMEC/D3, 1-BEC	BMEC, CoAEC	glutathione	X	✓ (negative)
156	$CoFe_2O_4$ (27 nm)	citrate	unspecified	Prussian blue staining, fluorescence microscopy	MDA-MB-231, MCF-7	X	citrate	✓	✓

158	Iron oxide (10 nm)	dimercapto-succinic acid (DMSA)	C2-N(H)-C(O)-	Prussian blue staining	MDA-MB-231	X	DMSA	X	✓
159	Iron oxide (10 nm)	dimercapto-succinic acid (DMSA)	C2-N(H)-C(O)-	Prussian blue staining	HeLa	X	DMSA	X	✓
160	Iron oxide (10 nm)	dimercapto-succinic acid (DMSA)	C2-N(H)-C(O)-	Prussian blue staining	MDA-MB-231, MCF-7	HMEpiC	DMSA	✓	X
161	Peptide amphiphile nanofibers & nanospheres	serine	C1-O-	fluorescence microscopy, flow cytometry	MCF-7	X	no ligand	X	✓ (negative)
c. Long linker between glucose and NP									
162	Au (13 nm)	18-bond thiol	C2-N(H)-C(O)-	fluorescence microscopy	RAW264.7 and peritoneal macrophages	X	zwitterionic thiol	X	X
163	CdTe/CdS QDs (4 nm)	sugar chain-phenyldiamene	C1-O-	Flow cytometry	HepG2	X	tetraethylene glycol	X	X
165	carbon dots (4 nm)	glucose-derived polymer	unspecified	fluorescence microscopy	Yeast BC	Yeast EBY.VW 5000	X	X	X
167	Iron oxide (10-30 nm)	polyglycerol	C2-N(H)-C(O)-	flow cytometry	LLC	16HBE	polyglycerol	X	X
132	mesoporous silica (200-400 nm)	PEI	C6(O)-N(H)-	fluorescence microscopy, flow cytometry	HeLa, A549	MEF	PEI	X	X
168	mesoporous silica (200-400 nm)	PEI	C6(O)-N(H)-	flow cytometry	MDA-MB-231	X	no ligand, PEI	X	X
133	MWCNTs	PEG (5k)	C2-N(H)-C(O)-	radiolabelling	MDA-MB-231	X	X	✓ (only minor effect)	(✓) (negative)

169	single-chain polymer NPs (1.9-3.4 nm)	X	C1-O-, C6-O-	fluorescence microscopy, flow cytometry	HeLa	X	X	X	X
170	polyether-copolyester dendrimers (7-11 nm)	PEG (400)	C2-N-C(O)-O-	fluorescence	U87-MG, U-343-MGa	X	no ligand	X	X
171	PAMAM dendrimers (12-20 nm)	X	unspecified	fluorescence, fluorescence microscopy	MDA-MB-231	HaCaT	no ligand	X	X
172	mesoporous silica/PAMAM (88 nm)	X	C6(O)-N(H)-	cell viability	Y79	X	no ligand	X	X
173	PLGA (100 nm)	N/A	C2-N(H)-C(O)-	fluorescence microscopy	HT-29	X	no ligand	X	X
174	PEG-PPO micelles (17 nm)	PEG (2.6 k)	C1(O)-O-	fluorescence microscopy, cell viability	Rh30	X	no ligand, galactose	X	X
175	PEG-PPO micelles (17 nm)	PEG (2.6 k)	C1(O)-O-	fluorescence microscopy, cell viability	Rh30	X	no ligand	(✓) (incon-clusive)	X
176	PEG-PPO micelles (6-50 nm)	PEG (2.6-4.4 k)	C1(O)-O-	fluorescence microscopy, cell viability	4T1	X	no ligand	X	X
177	TiO_2/PEG-PPO (30-300 nm)	PEG (2.6 k)	C1(O)-O-	fluorescence microscopy, flow cytometry	Rh30	X	no ligand	X	X
92	Iron oxide NPs/PEG-PCL micelles (35nm)	PEG (~4k)	C2-N(H)-C(O)-	FAAS	PC-3	X	methoxyethyl	X	X
178	PEG-PCL micelles (22nm)	PEG (~4k)	C2-N(H)-C(O)-	fluorescence microscopy	HepG2, MCF-7, PC-3	L929	methoxyethyl	X	X

80	PEG-p(EHGE-FGE) worm-like micelles	PEG (4k)	C6-S-	fluorescence microscopy, flow cytometry	MDA-MB-231, U87-MG	X	PEG	X	X
179	Soluplus® copolymer-based micelles (110 nm)	PEG	C1(O)-O-	drug release (HPLC)	MCF-7, MDA-MB 231	X	PEG	X	X
180	1-tetradeca-nol/cholesterollipidNPs (20-40 nm)	poly(2-oxazoline)s	C6-O-	fluorescence microscopy, flow cytometry	PC-3, MDA-MB-231	X	poly(2-oxazoline)s	✓ (negative)	X
181	PEG/lipid/cholesterol nanodisks (50 nm)	7-residue peptide	C1-O-	fluorescence microscopy, flow cytometry	bEnd.3	U87	no ligand, non-glyconjugated peptide	X	X
183	PEG/lipid/cholesterol nanodisks (50 nm)	7-residue peptide	C1-O-	fluorescence microscopy, flow cytometry	bEnd.3	X	X	✓ (incon-clusive)	X
185	LIPs (100 nm)	$C_{14}O_6N$	C6-O-	flow cytometry	bEnd.3, C6	X	no ligand	(✓) (incon-clusive)	X
186	LIPs (120 nm)	$C_{17}O_9$	C6-O-	fluorescence microscopy, flow cytometry	bEnd.3, C6	L02	no ligand	(✓) (incon-clusive)	X
187	LIPs (80-100 nm)	PEG	C6-O-	fluorescence	BBB model	X	no ligand	X	X
188	LIPs (125 nm)	PEG (2k)	C1-O-	fluorescence microscopy, flow cytometry	GL-261, bEnd.3	X	no ligand	X	X
189	Au (11 nm) silica (~100 nm) PEG-PLGA copo-lymer (~35 nm)	PDA/PEG (5k)	C6-O-	fluorescence microscopy, ICP-MS	bEnd.3	X	PDA/PEG	X	✓

113	Au (20 nm)	polyion-PEG (2k)	C6-O-	flow cytometry	MDA-MB 231	X	mPEG	X	✓
78	Au (20 nm)	PEG (0.35k)	C1-N(H)-C(O)- C2-N(H)-C(O)- C3-N(H)-C(O)- C6-N(H)-C(O)-	FAAS	A431	3T3	X	✓	✓
88	Au (20 nm)	PEG (0.35k	C1-N(H)-C(O)- C2-N(H)-C(O)-	fluorescence microscopy, FAAS	A431, A549	3T3, LNCaP	X	X	✓
190	AuNP (5-20 nm)	PEG (0.35k)	C2-N(H)-C(O)-	FAAS, microscopy	exosomes derived from MSC	X	mPEG	✓	✓
44	Gd_2O_3@oval-bumin	PEG (1k)-maleimide-mercaptoun-decanoic acid	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	bone marrow-derived dendritic cells	X	no ligand	X	✓
191	CdTe QDs (3nm)/lipoic acid-Lys-Arg_9 (130 nm)	PEG (2k)	C2-N(H)-C(O)-	fluorescence microscopy	HepG2	U87-MG	no ligand	✓	X
192	CdSe/ZnS core-shell QDs (8 nm)	DHLA-TEG	C1-O-	fluorescence microscopy, flow cytometry	differentiated C2C12	X	DHLA-TEG	✓	X
193	$CaMgSiO_3$ (20-30 nm)	PAMAM	not specified	fluorescence	WEHI-164	3T3	X	✓	X
194	PAMAM conjugates (43 nm)	PEG	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	MCF-7	L02	no ligand, mPEG	✓	X

195	PAMAM conjugates (13 nm)	PEG (5k)	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	HepG2	L02	no ligand, mPEG	✓	X
196	PAMAM conjugates (13 nm)	succinyl	C6-C(O)-	cell viability	MCF-7	X	no ligand	(✓)	✓
90	Glucose-PLGA (240 nm)	N/A	C1-O-, C2-O-, C3-O-, C4-O-, C6-O- (mix)	fluorescence microscopy, flow cytometry	Hep-2	X	PLGA NPs	✓	X
111	PEG-PTMC copolymer (71 nm)	PEG (3k)	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	RG-2, bEnd.3	X	no ligand	✓	✓
198	PEG-PTMC copolymer (71 nm)	PEG (3k)	C2-N(H)-C(O)-	cell viability	RG-2	X	no ligand	X	X
199	Polydopamine (PDA)	direct, diethylene glycol	C2-N-, C1-O-	cell viability, fluorescence microscopy	MDA-MB-231	MCF-10A	no ligand	✓	✓
98	antibody-siRNA conjugate in pAPMAAnano-capsule (100 nm)	APBA	C3-O-+C4-O-	fluorescence microscopy	bEnd.3, U87	X	APBA	✓	X
200	P105 polymeric micelles (25 nm)	PEG (1.5k)	C6-O-	fluorescence	BBB model, C6	X	no ligand, folic acid	✓	X
201	LIPs (110 nm)	PEG (2k)	C1-O-	fluorescence microscopy, flow cytometry	murine BCECs, BBB model	U251	no ligand, RGD peptide	✓	X

40	PEG-polyion polymeric micelles (30nm)	PEG (2k)	C3-O-, C6-O-	fluorescence	Neuro2a cotransfectedwith GLUT1 ex-pressing plasmid	Neuro2a	no ligand	X	✓
110	PEG-polyion polymeric micelles (45nm)	PEG (5k)	C6-O-	fluorescence	MDA-MB-231	X	no ligand	X	✓
112	PEG-polyion polymeric micelles (45nm)	PEG (5k)	C6-O-	fluorescence	Caco-2, primary rat brain endo-thelial cells	X	no ligand	X	✓
119	PEG-poly(glutamic acid)-cisplatin micelles (30nm)	PEG (12k)	C6-O-	cell viability	OSC-19	U87-MG	no ligand	✓ (*in vivo*)	✓
202	phospholipid/ PEG vesicles (100 nm)	PEG (2k)	C2-N(H)-C(O)-	fluorescence microscopy, flow cytometry	C6/TR, bEnd.3	X	mPEG	X	✓
203	LIPs (66-120 nm)	ginsenoside Rg-3	C1-O-	fluorescence microscopy, flow cytometry	C6, BCEC, HUVEC	X	cholesterol	✓	✓
204	LIPs (125 nm)	PEG (2k)	C2-N(H)-C(O)-	ICP-OES, fluorescence microscopy	A431, A549, B16, 4T1, PC-3	LNCaP, 3T3	PEG-COOH	✓	✓
140	LIPs (125 nm)	PEG (2k)	C2-N(H)-C(O)-	ICP-OES	A431, 4T1, MDA-MB-231	3T3	PEG-COOH, PEG-Mannose	X	X

Abbreviations: AgNP, silver nanoparticle; APBA, (3-acrylamidophenyl) boronic acid; AuNP, gold nanoparticle; BBB, blood–brain barrier; DHLA, dihydrolipoic acid; DMSA, dimercaptosuccinic acid; FAAS, flame atomic absorption spectroscopy; GLUT, glucose transporter; HPLC, high-performance liquid chromatography; ICP-MS, inductively coupled plasma mass spectrometry; ICP-OES, inductively coupled plasma optical emission spectrometry; LIPs, phospholipid/cholesterol liposomes; mPEG, methoxy-polyethylene glycol; MWCNTs, multi-wall carbon nanotubes; NP, nanoparticle; PAMAM,

poly(amidoamine); pAPMAA, poly(3-aminopropyl methacrylamide); PCL, polycaprolactone; PDA, polydopamine; PEG, polyethylene glycol; PEG-COOH, carboxy(polyethylene glycol); p(EHGE-FGE), poly(2-ethylhexyl glycidyl ether-co-furfuryl glycidyl ether); PEI, poly(ethylene imine); PEO, poly(ethylene oxide); PLGA, poly(lactic-co-glycolic acid); PMAO, poly(maleic anhydride-alt-1-octadecene); PPO, polypropylene oxide; PTMC, poly(trimethylene carbonate); P105, pluronic block copolymer containing PEO and PPO; QDs, quantum dots; RGD, arginine-glycine-aspartic acid; siRNA, small interfering RNA; TEG, tetra(ethylene glycol); TEM, transmission electron microscopy; TMZ, temozolomide;3-MPS, 3-mercapto-1-propanesulfonate.

Cell lines: A2780, human ovarian cancer; A431, human epidermoid carcinoma; A549, human lung adenocarcinoma; BCEC, brain capillary endothelial cells; BC, yeast barcode strain derived from BY4709; bEnd.3, murine brain endothelial cells; BMEC, brain microvascular endothelial cells;B16, murine melanoma; Caco-2, human colorectal adenocarcinoma; CoAEC, brain microvascular endothelial cells; C2C12, murine muscle; C6, murine glioma; C6/TR, TMZ-resistant C6 cells; DU-145, human prostate carcinoma; EBY.VW5000, hexose-transport-negative yeast strain; GL-261, murine glioblastoma; HaCaT, human keratinocytes; hCMEC/D3, human cerebral microvascular endothelial cells; HEK293T, human embryonic kidney; HeLa, human cervical carcinoma; HepG2, human hepatocellular carcinoma; Hep-2, human epithelial carcinoma; HHL5, human-derived hepatocyte; HMEpiC, human mammary epithelial cells; HSG, human salivary gland; HT1080, human fibrosarcoma; HT-29, human colorectal adenocarcinoma; HUVEC, human umbilical vein endothelial cells; LLC, Lewis (murine lung cancer) cells; LNCaP, human prostate adenocarcinoma; L02, normal human liver cells; L929, mouse fibroblast; MCF-7, human breast adenocarcinoma; MCF-10A, non-tumorigenic mammary epithelial cells; MDA-MB-231, human breast adenocarcinoma; MDCK, immortalized kidney cells; MEF, mouse embryonic fibroblasts; MKN-45, gastric cancer; MSC, mesenchymal stem cells; Neuro2a, mouse neuroblastoma; OSC-19, human oral squamous cell carcinoma; PC-3, human prostate adenocarcinoma; RAW264.7, murine macrophages; RG-2, murine glioma; Rh30, human rhabdomyosarcoma; SK-MEL-28, human melanoma; SK-OV-3, human ovarian cancer; SVG p12, human foetal glial cells; SW1990, human pancreatic carcinoma; THP-1, human leukaemia; U251, human glioblastoma; U343-MGa, human glioblastoma; U87/U87-MG, human glioblastoma; Vero, African green monkey kidney epithelial cells; WEHI-164, murine fibrosarcoma; Y79, human retinoblastoma; 1-BEC, brain microvascular endothelial cells; 16HBE, human bronchial epithelial cells; 3T3, murine embryonic fibroblast; 4T1, murine mammary carcinoma.

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