Polymerization-induced self-assembly of galactose-functionalized biocompatible diblock copolymers for intracellular delivery

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Polymerization-induced self-assembly

Note: Targeting relatively long PHPMA blocks at 10 % solids produced a mixture of spheres and small vesicles. These spheres are believed to be kinetically-trapped copolymer morphologies. However, no evidence for a sphere-to-vesicle transformation was observed during the long-term storage of these samples at 20 °C for five months.

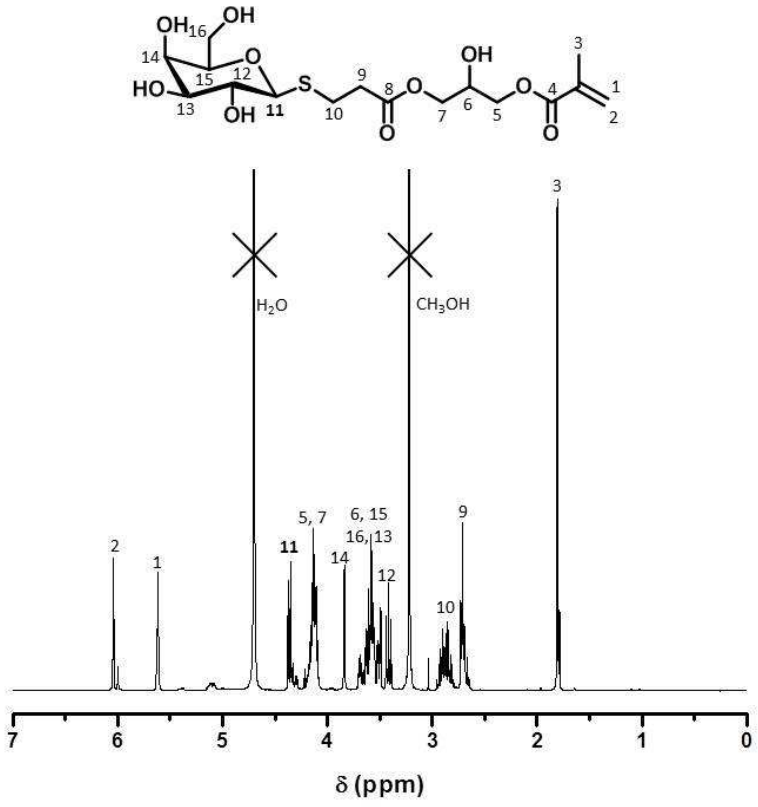

Figure S1. Assigned ^{1}H NMR spectrum recorded for galactose methacrylate monomer dissolved in D_2O at 20 ^{o}C.

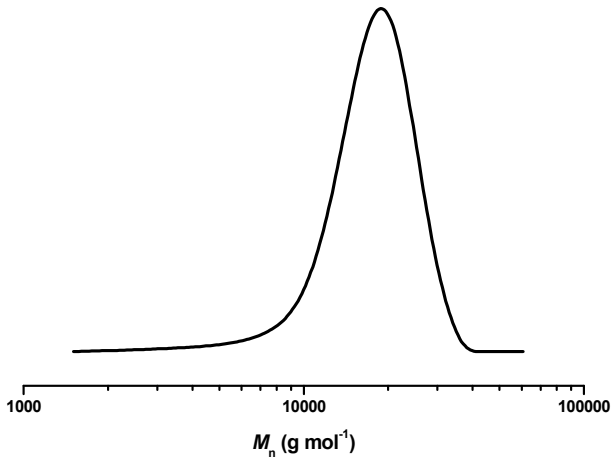

Figure S2. DMF GPC curve obtained for $PGalSMA_{34}$ at 60 °C (M_n = 16,300 g mol^{-1}, M_w = 18,500 g mol^{-1}, M_w/M_n = 1.13). RAFT synthesis conditions: [GalSMA] : [PETTC] : [ACVA] = 30 : 1 : 0.1; 25 % w/w GalSMA in a 9:1 mixture of PBS buffer (150 mM, pH 7.2) and methanol. Monomer conversion = 97 %.

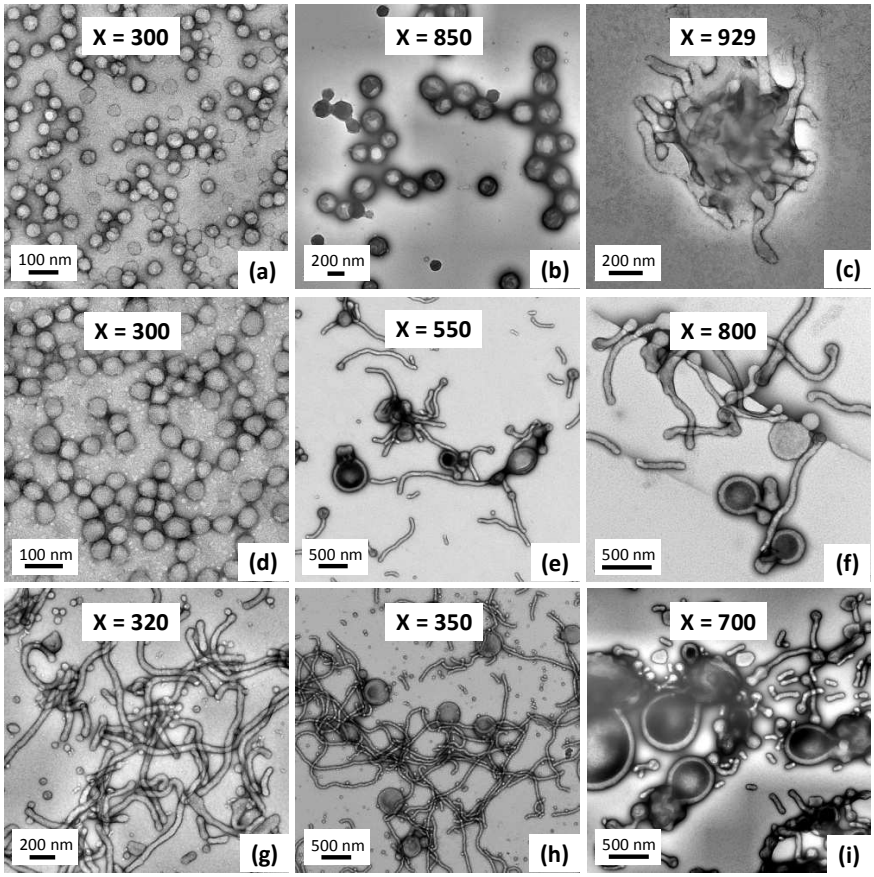

Figure S3. Representative TEM images obtained for $PGalSMA_{34}$-$PHPMA_x$ diblock copolymer nano-objects synthesized by RAFT aqueous dispersion polymerization of HPMA at 70 °C. The target DP (x) for the PHPMA block is indicated on each image. Images (a), (b) and (c) shown the morphologies obtained at 10 % solids; images (d), (e) and (f) refer to morphologies formed at 15 % solids; images (g), (h) and (i) were produced at 20 % solids.

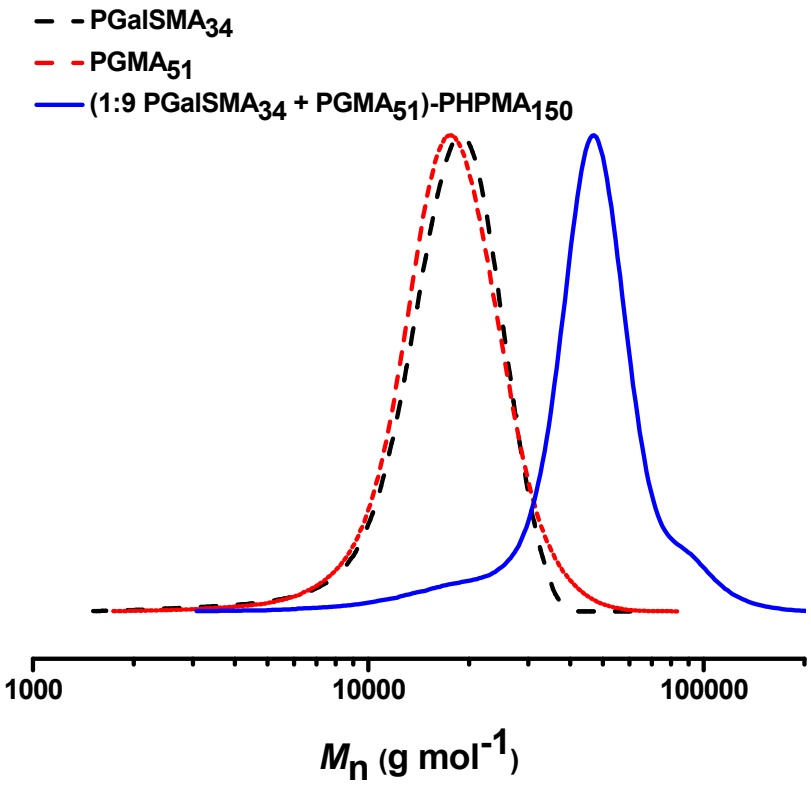

Figure S4. Representative DMF GPC traces of the $PGalSMA_{34}$ (M_n = 16,300 g mol^{-1}, M_w = 18,500 g mol^{-1}, M_w/M_n = 1.13) and $PGMA_{51}$ (M_n = 16,200 g mol^{-1}, M_w = 18,600 g mol^{-1}, M_w/M_n = 1.15) macro-CTAs and the corresponding (1:9 $PGalSMA_{34}$ + $PGMA_{51}$)–$PHPMA_{150}$ (M_n = 38,700 g mol^{-1}, M_w = 47,100 g mol^{-1}, M_w/M_n = 1.21) diblock copolymer obtained at 20 % solids content.

Solids content (%)	DP_{HPMA} Targeted	Conversion (%)	M_w (g mol^{-1})	M_n (g mol^{-1})	M_w/M_n
10	90	>99	35,300	30,500	1.15
10	150	>99	48,000	41,200	1.16
10	200	>99	51,100	42,000	1.22
10	270	>99	70,700	56,500	1.25
15	90	>99	35,500	31,000	1.14
15	150	>99	46,100	38,400	1.20
15	200	>99	57,400	48,200	1.19
15	270	>99	72,500	58,500	1.24
20	90	>99	36,400	31,600	1.15
20	150	>99	47,100	38,700	1.21
20	200	>99	57,800	48,000	1.20
20	270	>99	70,300	55,400	1.27

Table S1. Molecular weights determined by DMF GPC for (1:9 $PGalSMA_{34}$ + $PGMA_{51}$)-$PHPMA_x$ diblock copolymers synthesized by RAFT aqueous dispersion polymerization.

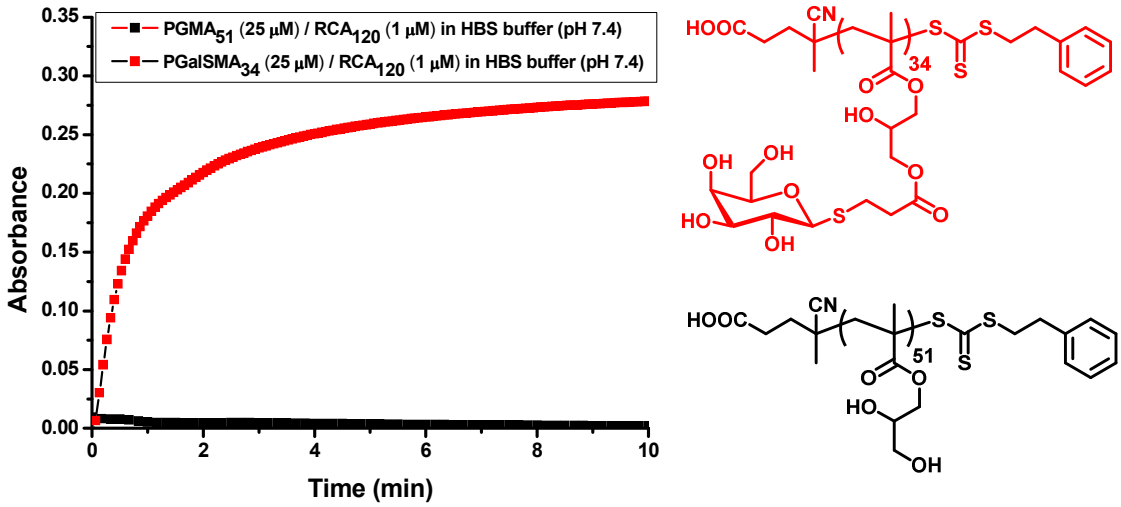

Figure S5. Lectin interaction control experiments. The $PGMA_{51}$ macro-CTA (black squares) is not recognized by RCA_{120}, hence no binding interaction occurs. In contrast, using $PGalSMA_{34}$ (red squares) under the same conditions leads to rapid aggregation in the presence of RCA_{120}.

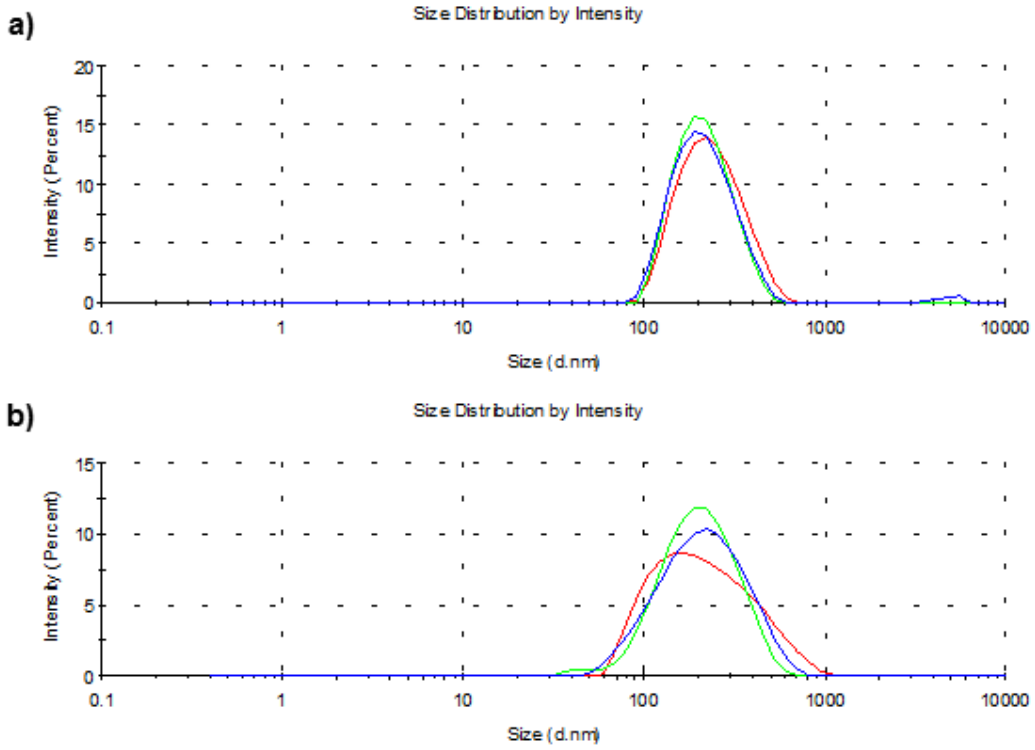

Figure S6. Dynamic light scattering particle size distributions for: a) vesicles obtained by PISA (intensity-average diameter, d = 231 ± 13 nm), b) vesicles obtained by film rehydration (d = 236 ± 15 nm). These measurements were performed using the same diblock copolymer binary mixtures, i.e. (1:9 $PGalSMA_{34}$ + $PGMA_{51}$)-$PHPMA_{270}$. The diameter is calculated from the average of three measurements in each case.

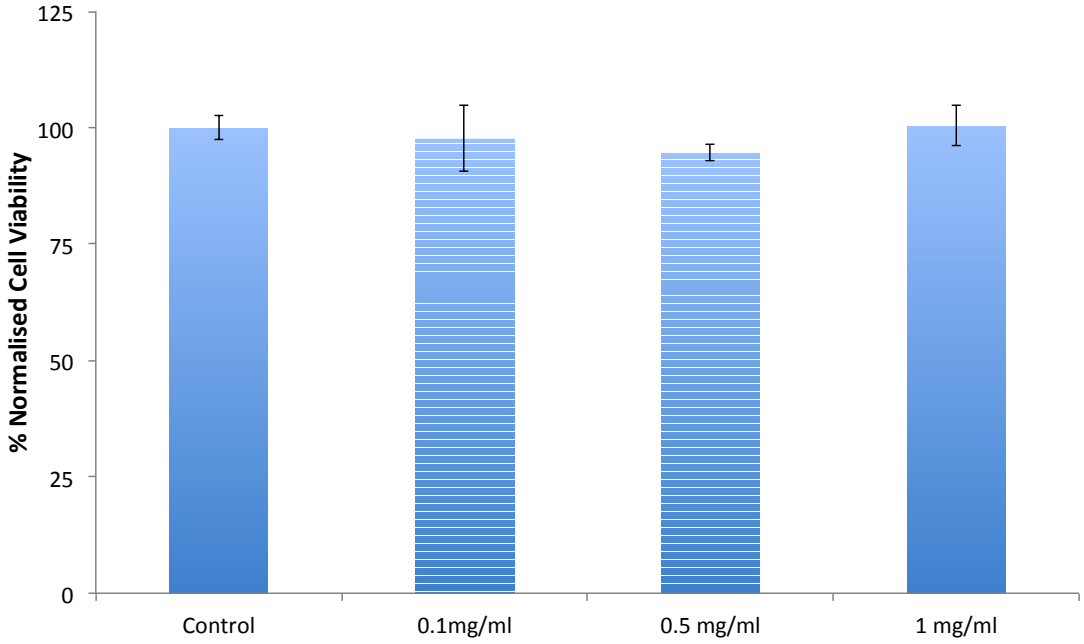

Figure S7. Normalized cellular viability of human dermal fibroblasts after incubation with (1:9 $PGalSMA_{34}$ + $PGMA_{51}$)-$PHPMA_{270}$ vesicles. Cells were incubated in the presence of increasing concentrations of vesicles in cell media over 24 h. Cell viabilities were evaluated using an MTT-ESTA assay and the data were normalized relative to the untreated control (100% viability). N = 3 independent experiments were performed in triplicate wells.