Electronic Supplementary Material (ESI) for Biomaterials Science.

Heparosan as a potential alternative to hyaluronic acid for the design of biopolymer-based nanovectors for anticancer therapy

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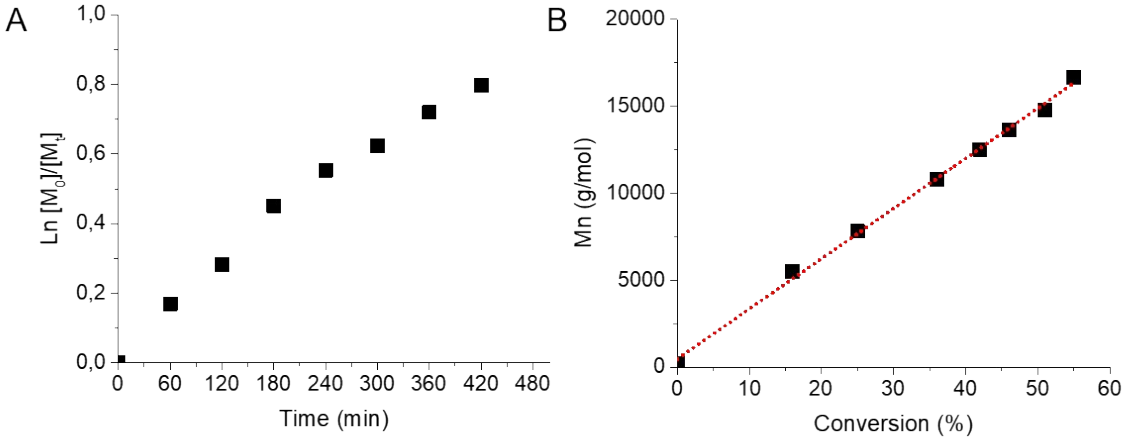

Figure S1. (A) Kinetic plots and (B) dependence of the number-average molar masses (M_n) on monomer conversion for the RAFT copolymerization of DEGMA and BMA. Reaction conditions: $[DEGMA]_0/[BMA]_0/[CTA]_0/[AIBN]_0 = 95/5/0.77/0.038$ at 80°C in toluene.

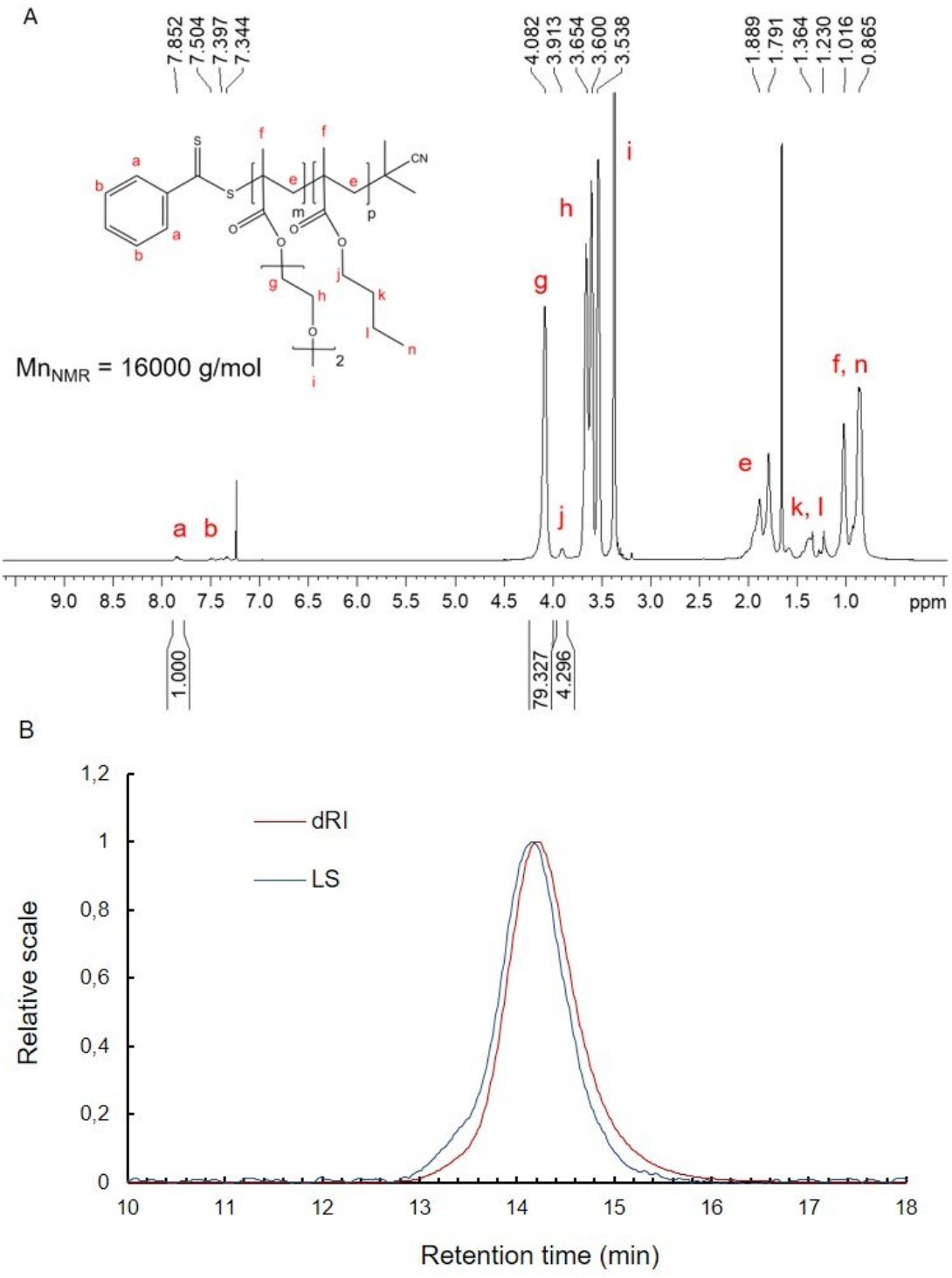

Figure S2. Characterisation of poly(DEGMA-co-BMA) by A) ^{1}H NMR spectroscopy (300 MHz, 10 mg/mL in $CDCl_3$ and, B) SEC at 30 °C and at a flow rate of 1 mL/min, in dimethylformamide containing 50 mM $NaNO_3$.

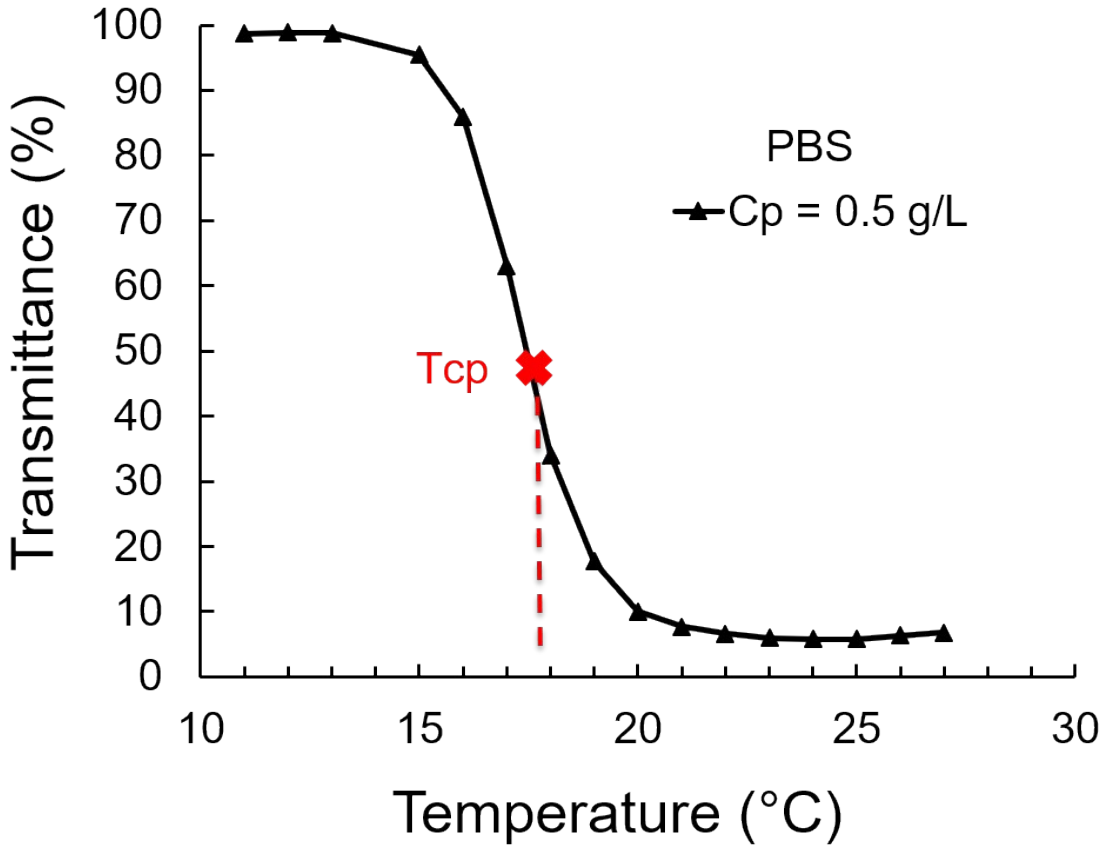

Figure S3. Turbidity measurement of a solution of poly(DEGMA-co-BMA) in PBS (0.5 g/L) as measured by UV/Vis spectroscopy at 500 nm.

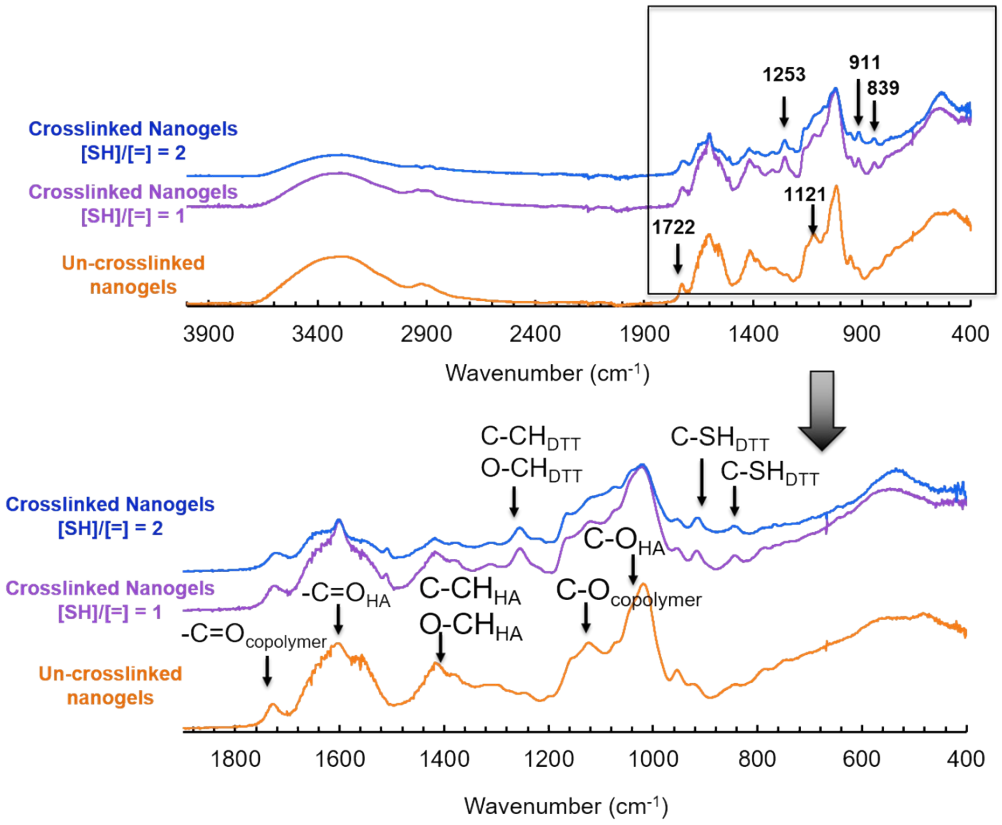

Figure S4. FT-IR spectra of crosslinked Hep-NGs with [SH]/[=] = 2 (blue) and [SH]/[=] = 1 (purple), and of un-crosslinked Hep-NGs (orange). Focus on the 1800-400 cm^{-1} region includes characteristic bands of DTT on the heparosan backbone.

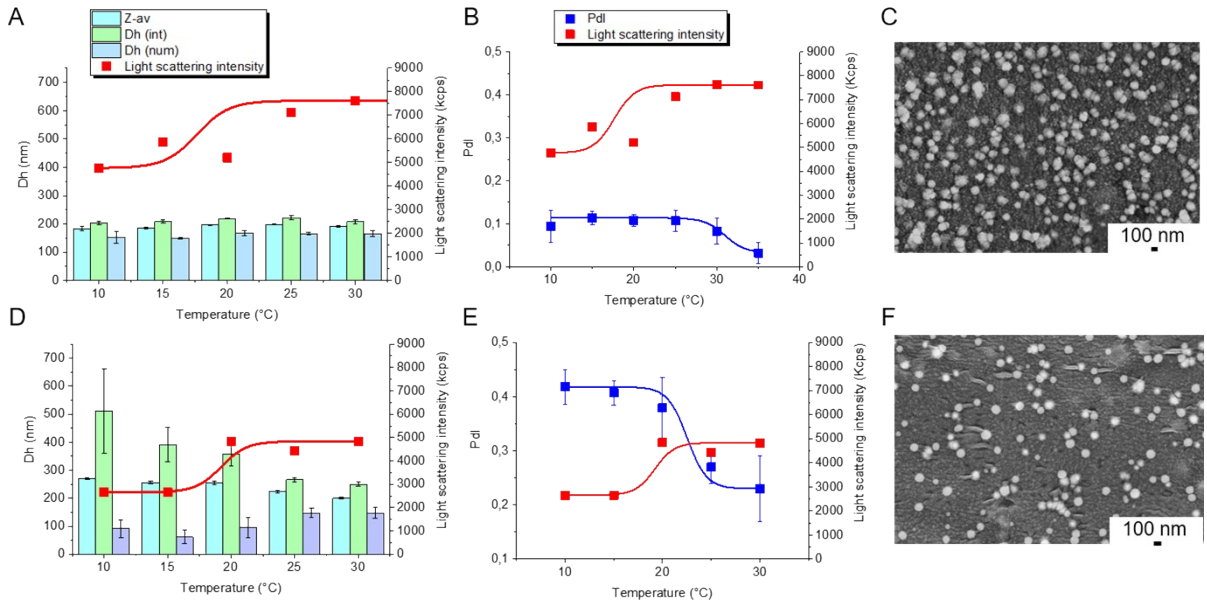

Figure S5. Behavior as a function of temperature of nanogels based on Hep-p-poly(DEGMA-co-BMA) and HA-p-poly(DEGMA-co-BMA) crosslinked with a [SH]/[=] ratio of 1. Analysis by DLS (C_p = 0.5 g/L in PBS) and by SEM of Hep NGs (A, B, C) and of HA NGs (D, E, F).

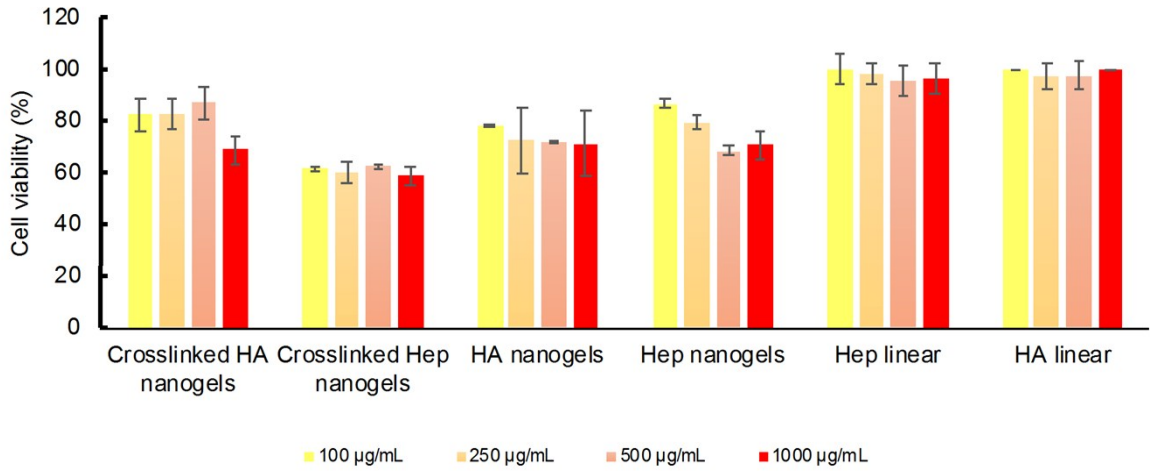

Figure S6. *In vitro* cytotoxicity of un-crosslinked and crosslinked HA- and Hep-NGs as well as of native HA and Hep in Vero cells after 72 h of incubation, evaluated by the MTT method. Data are expressed as mean ± SD of three independent experiments.

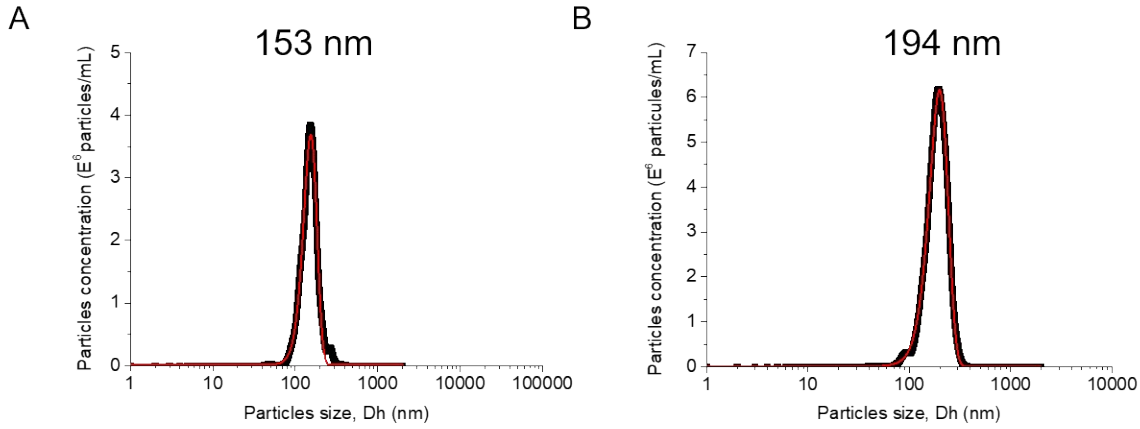

Figure S7. Size distribution of shell-crosslinked HA NGs (A) and Hep NGs (B) in PBS (C_p = 5×10^{-4} g/L) determined by nanoparticle tracking analysis at 25 °C. The experimental results (black curve) were fitted by a Gaussian curve (red curve).

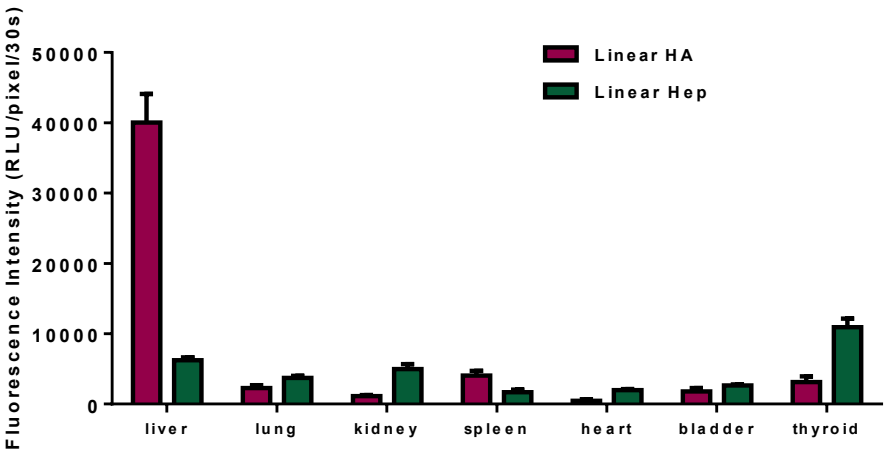

Figure S8. Quantification of the *ex vivo* biodistribution of Cy7-labeled initial HA40 and Hep30 in normal mice 24 h after administration (n = 3/organ). The results in each organ are expressed as the mean of relative light unit ± SD (n=3).