Supporting Information

Preparation of hyaluronic acid nanoparticles via hydrophobic association assisted chemical cross-linking – an orthogonal modular approach

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Scheme S1. Loading of free DOX (a) and its hydrochloride salt (b) into cross-linked HA NPs.
**Fig. S1.** UV-vis spectra of the cross-linked HA NPs with DS = 5 % (solid curve) and 0.5 % (dotted curve) in DMSO (concentration of NPs was 0.1 mg/mL). DS is defined as the number of pyrene units per 100 HA disaccharide units. Inserts: photographs of the aqueous dispersions of the cross-linked HA NPs with DS = 0.5 % (left vial) and 5 % (right vial) as seen in day light and UV light.
**Fig. S2.** SEM images of cross-linked HA NPs with DS = 0.5%.
**Fig. S3.** Standard calibration curves of doxorubicin in acetone-water mixture (4:1, v/v) (▼) and in PBS buffer (pH 7.4) (●).

The change of absorbance (curve slope) of DOX at 490 nm in acetone-water mixture ($\text{Abs}_{490\text{nm}} = 0.0223[C]_{\text{DOX}} + 0.0431$, $R^2 = 0.998$) was much more faster than in PBS ($\text{Abs}_{490\text{nm}} = 0.0062[C]_{\text{DOX}} - 0.0016$, $R^2 = -0.999$).
Fig. S4. SEM images and particle size distribution of the cross-linked HA NPs (DS = 5%) loaded with free DOX (a, c) and DOX hydrochloride (b, d).