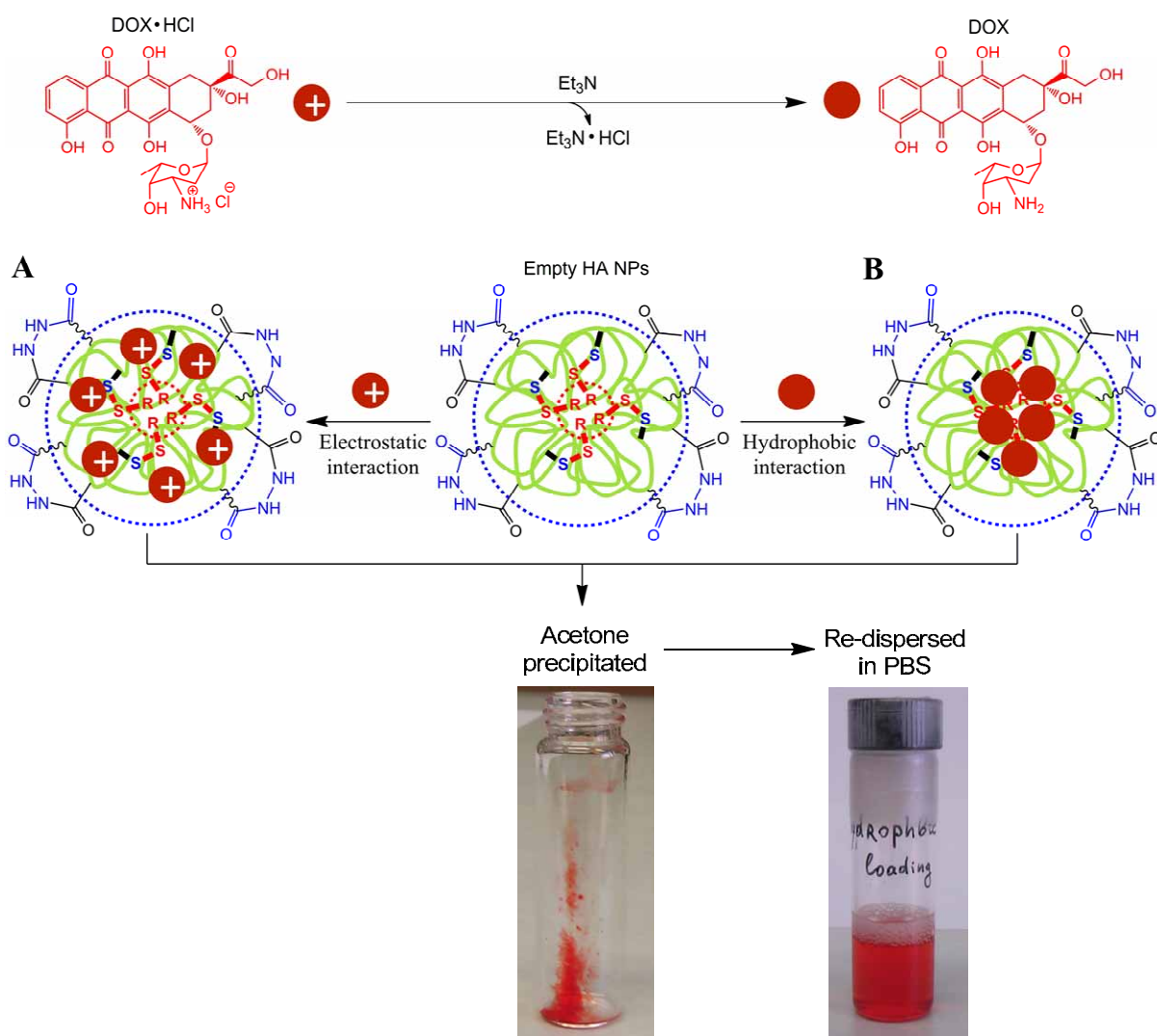


## Supporting Information

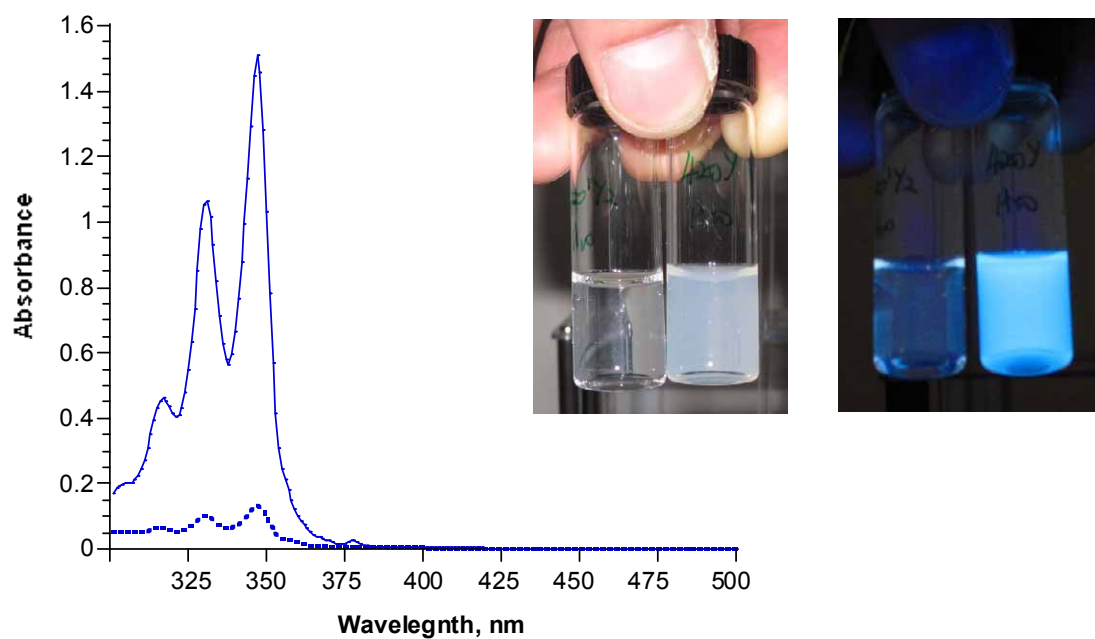
### **Preparation of hyaluronic acid nanoparticles via hydrophobic association assisted chemical cross-linking – an orthogonal modular approach**

*Xia Yang, Sujit Kootala, Jöns Hilborn, Dmitri A. Ossipov\**

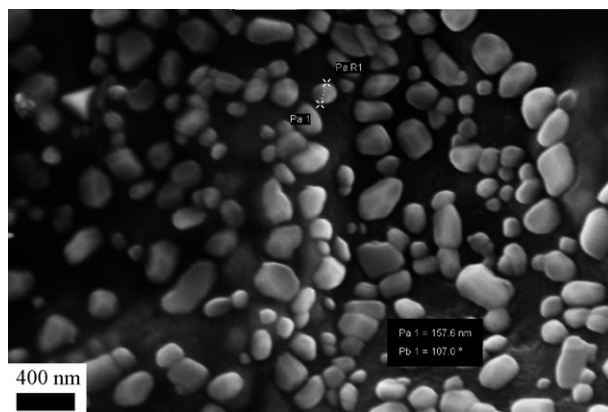
Department of Material Chemistry, Uppsala University, Ångström Laboratory, SE-75121, Uppsala,  
Sweden



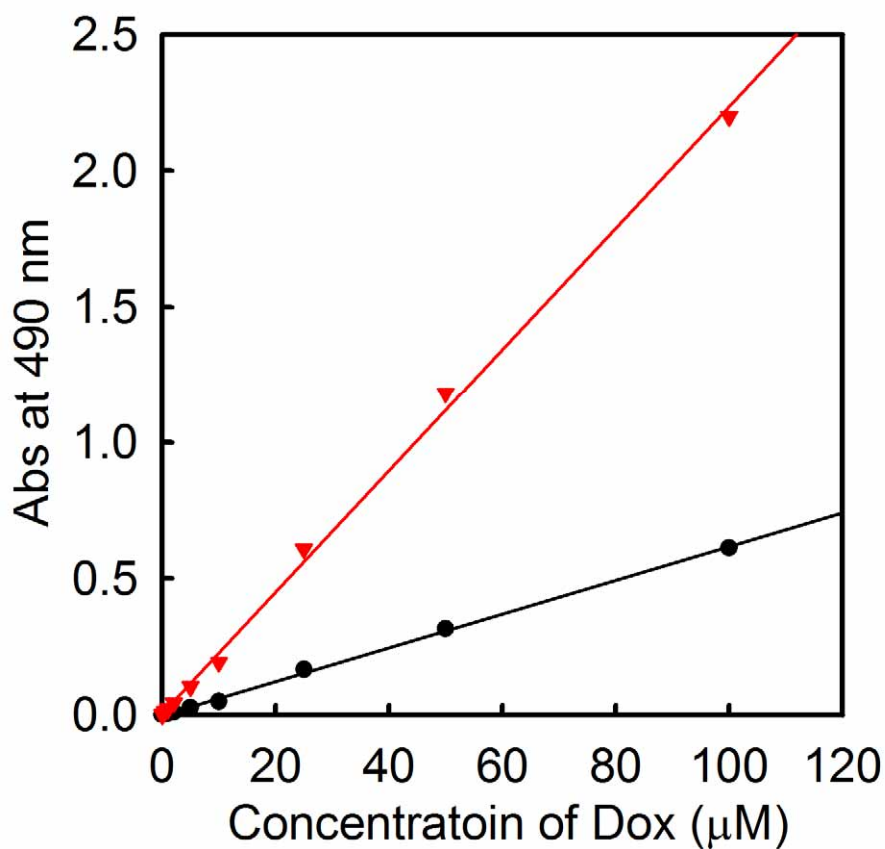
**Scheme S1.** Loading of free DOX (a) and its hydrochloride salt (b) into cross-linked HA NPs.



**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.

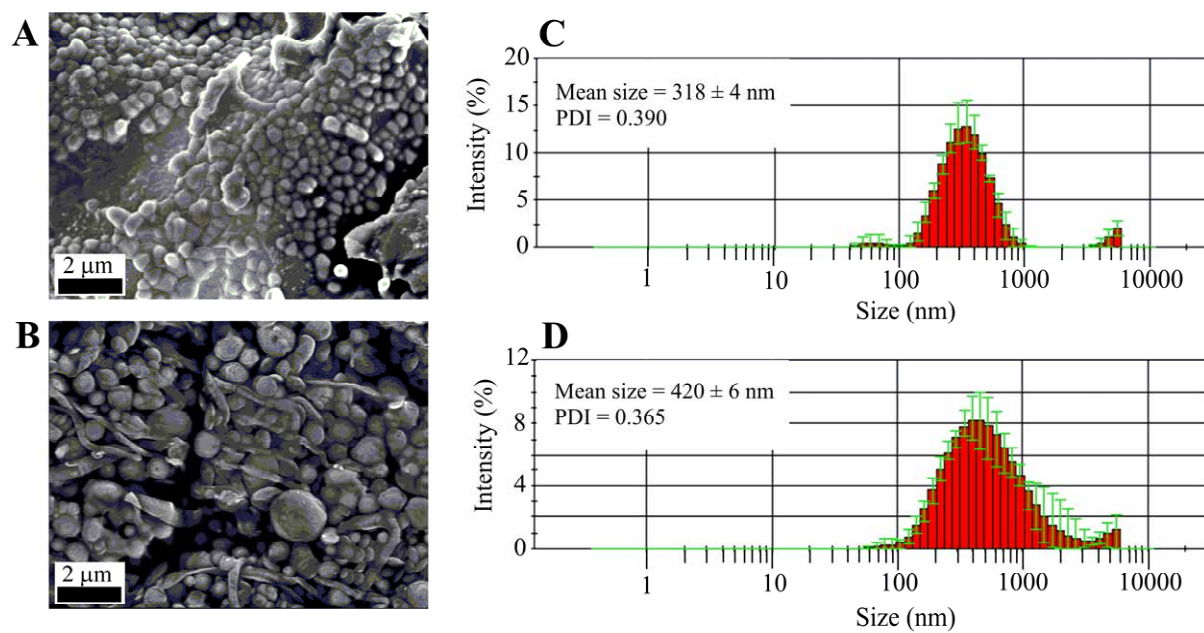


**Fig. S2.** SEM images of cross-linked HA NPs with DS = 0.5%.



**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 ( $Abs_{490nm} = 0.0223[C]_{DOX} + 0.0431$ ,  $R^2 = 0.998$ ) was much more faster than in PBS ( $Abs_{490nm} = 0.0062[C]_{DOX} - 0.0016$ ,  $R^2 = -.999$ ).



**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).