Supporting Information

Hyaluronic Acid Nanogel for Photo-Chemo Theranostic of Lung Cancer with Simultaneous Light-Responsive Controlled Release of Doxorubicin

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***In vitro* stability.** The *in vitro* stability of GDH was observed in PBS, pH 5 and 10% FBS solutions (Figure S3). We have used PBS to compare the stability in normal condition and in pH 5 as we know that the crosslink HA-SH easily breakdown in lower pH solutions and ester bond also breakdown in acidic pH due to hydrolysis and in 10% FBS to compare the stability of the formulations in body fluid condition. In this study, we have observed both size stability and fluorescence intensity up to 7 days of incubation. In case of particle size stability in PBS, no big difference of size was observed but after 5 days the particle size is reduced by breakdown of HA-SH network. In pH 5, the GDH size was started to reduce after 1 day, and day-by-day the particle size became smaller which may cause by breakdown of –SH and ester bonds. In 10% FBS condition the particle size is almost similar with PBS condition which may confirmed that our GDH is stable in FBS. The fluorescence intensity was decreased in pH 5 than PBS and FBS solutions. The phenomenon is same as like as size changes.

Fig S1. FT-IR spectrum of hyaluronic acid (HA), thiolated hyaluronic acid (HA-SH), doxorubicine conjugated graphene (DOX-Graphene) and HA-SH wrapped DOX-Graphene nanogel.

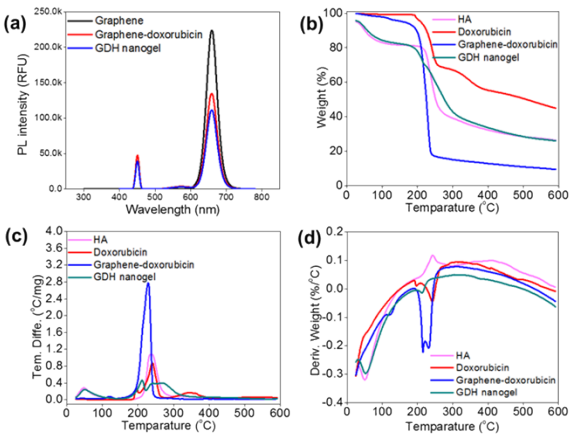

Fig S2. Fluorescence intensity and thermal stability of the nanogel measured by (a) spectrofluorometry, (b) thermogravimetric analysis, (c) differential thermal analysis and (d) differential scanning colorimetry.

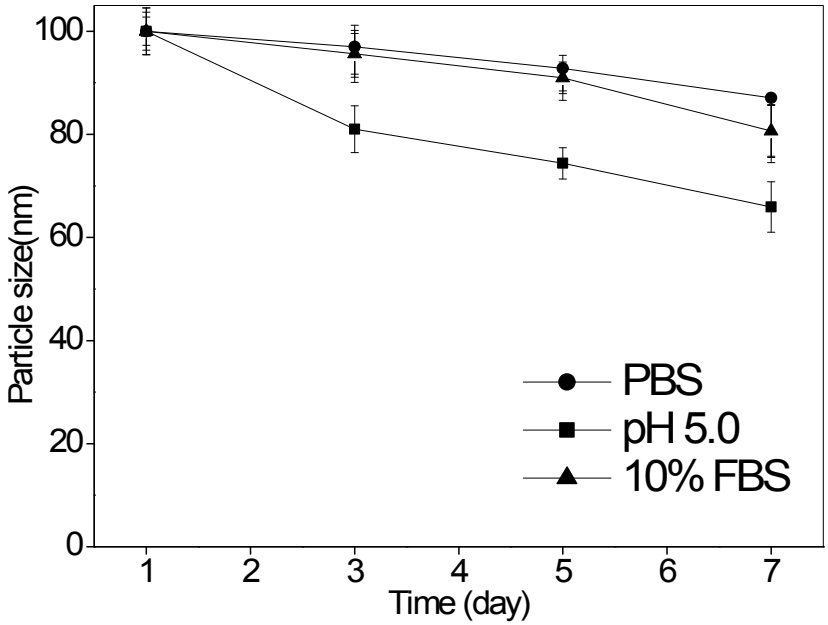

Fig S3. Size stability of nanogel in PBS, pH 5 and 10% FBS solution for 7 days of observation.

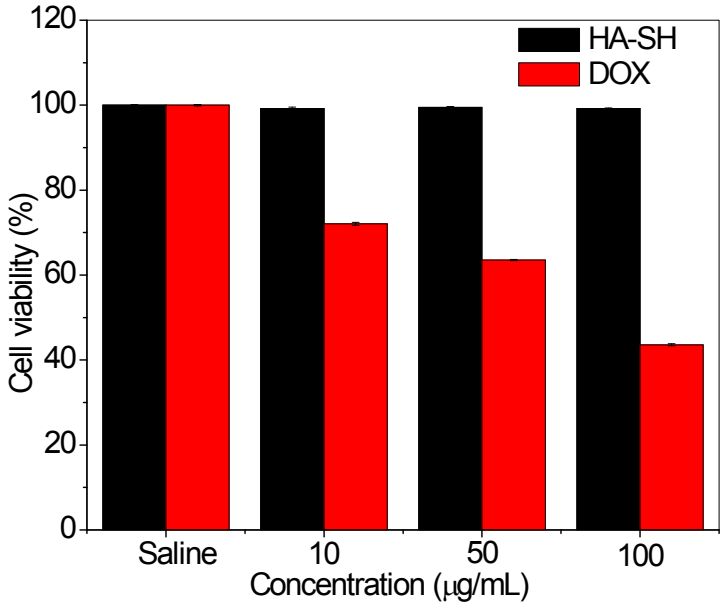

Fig S4. Cell cytotoxicity of HA-SH and DOX observed in A549 cell line for 24 h of incubation at different concentrations.

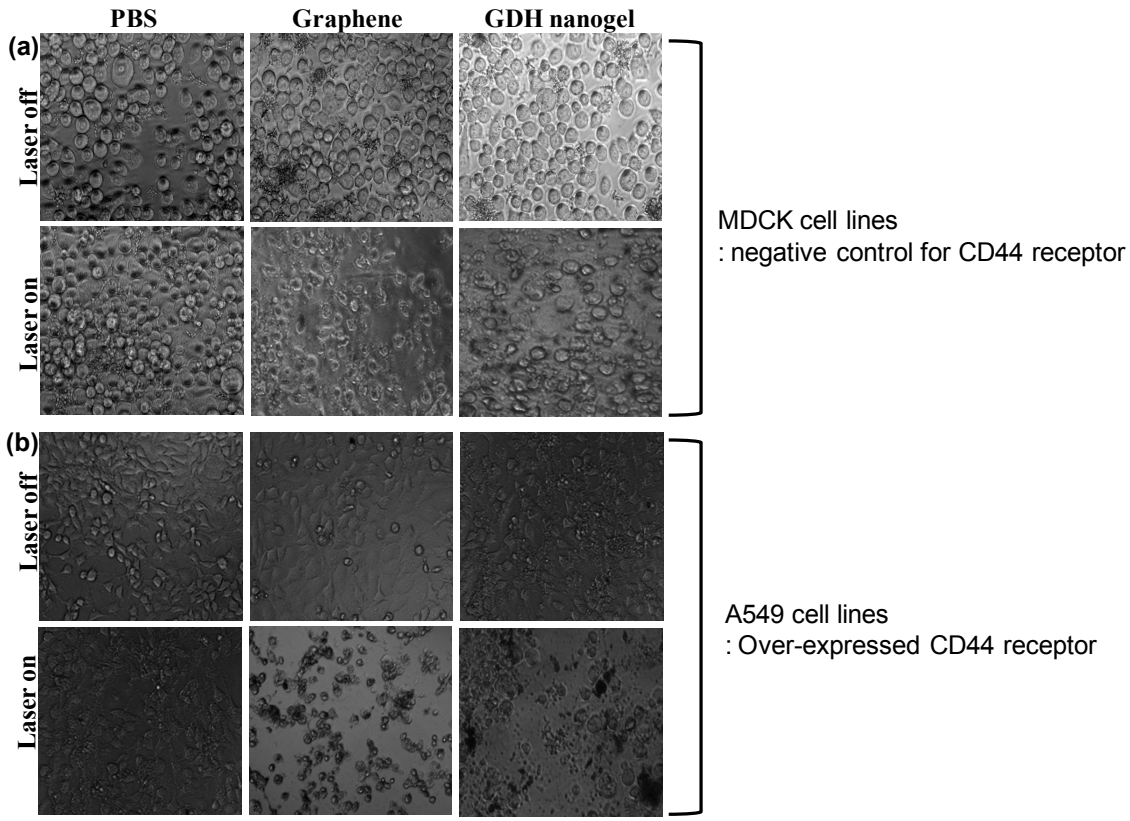

Fig S5. Visual images of cell viability of PBS, Graphene and nanogel (50 μg/mL) solution treated with MDCK cells (not expressed CD44 receptor) (a), and A549 cells (over expressed CD44 receptor) (b), were exposed to the 670 nm laser (1 W/cm^2) for 5 min captured after 24 h.

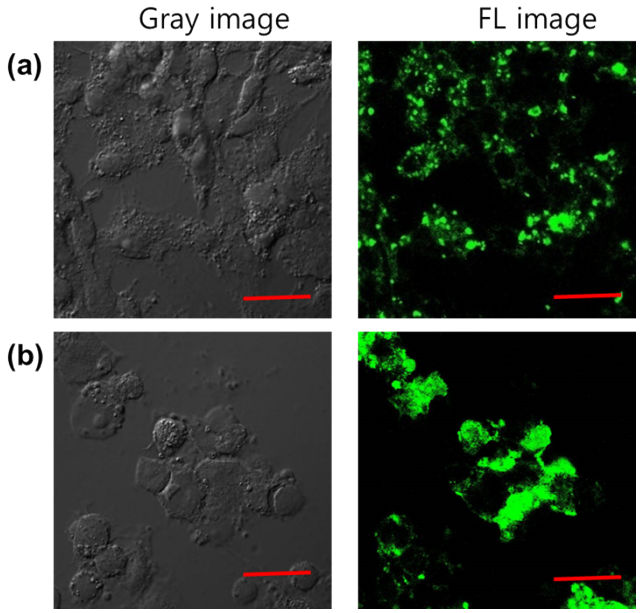

Fig S6. Confocal images of GQDs (a) and GDH nanogel (b) in A549 cell for 4 h of co-incubation at 10 μg/mL concentration. Scale bar= 50 μm.

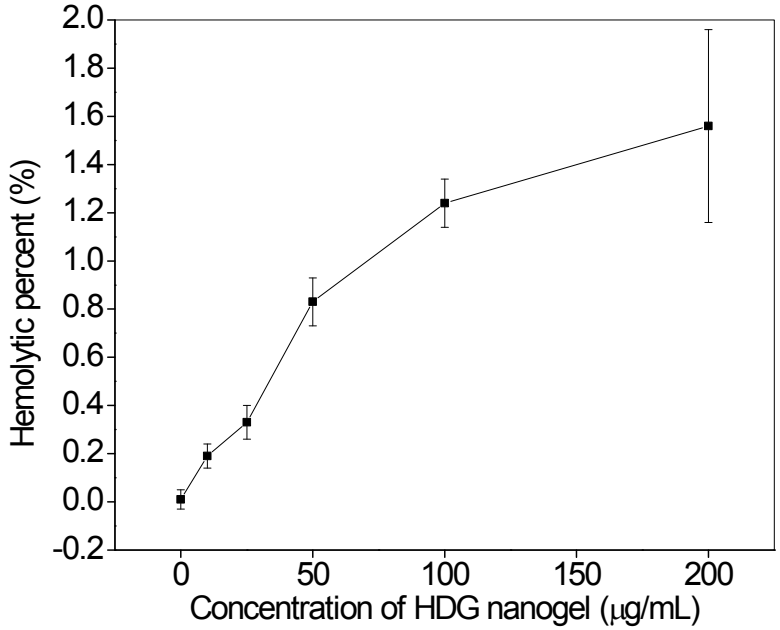

Fig S7. Hemolytic effect of GDH nanogel was observed in blood collected from rat at different concentration shows that concentration at 200 μg/mL has a hemolytic effect of 1.5%. The data was plotted as mean±SEM, where n=3

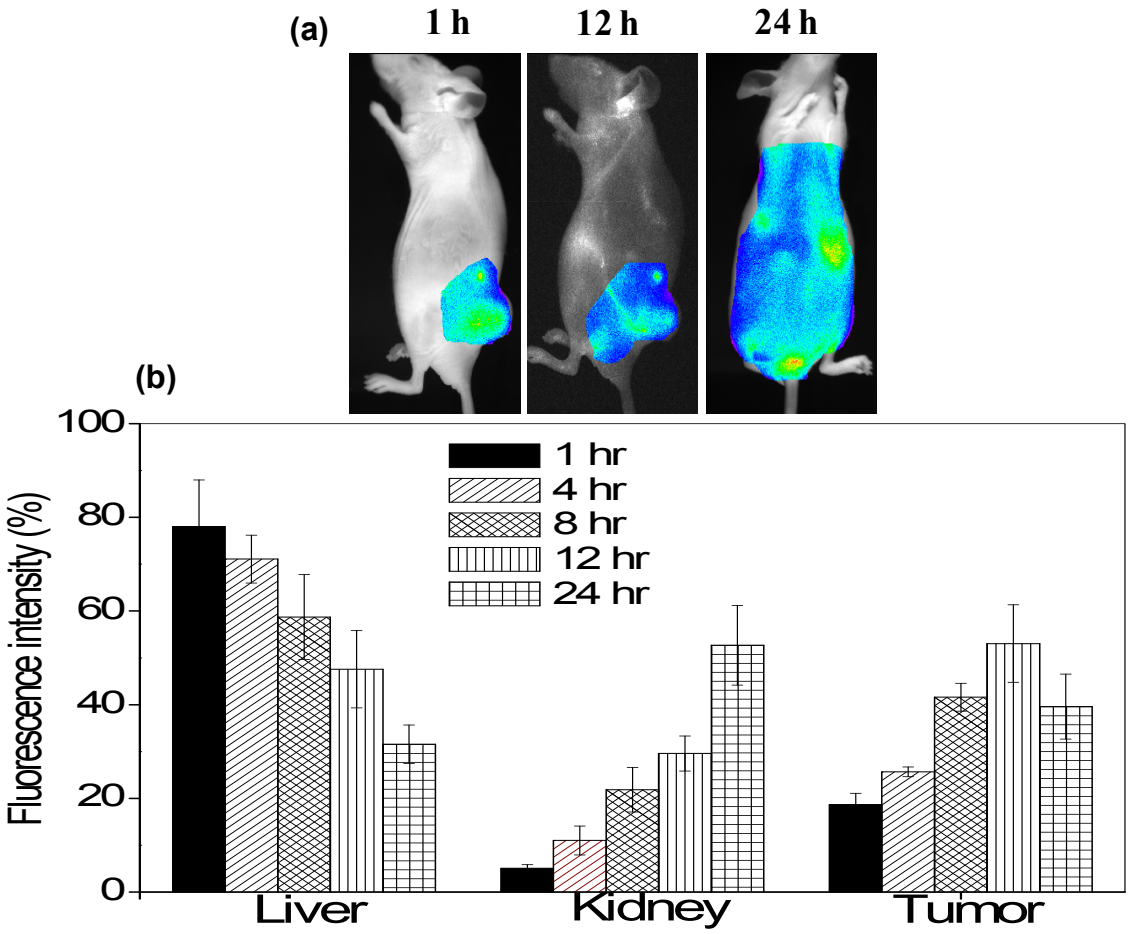

Fig S8. *In vivo* noninvasive images of nanogel injected nude mice (a), and biodistribution of mice organ fluorescence intensity treated with HA-GQDs-DOX solution at a concentration of 2.5 mg/mL. The mice were dissected at different time intervals and homogenized with homogenizer and check the fluorescence intensity.

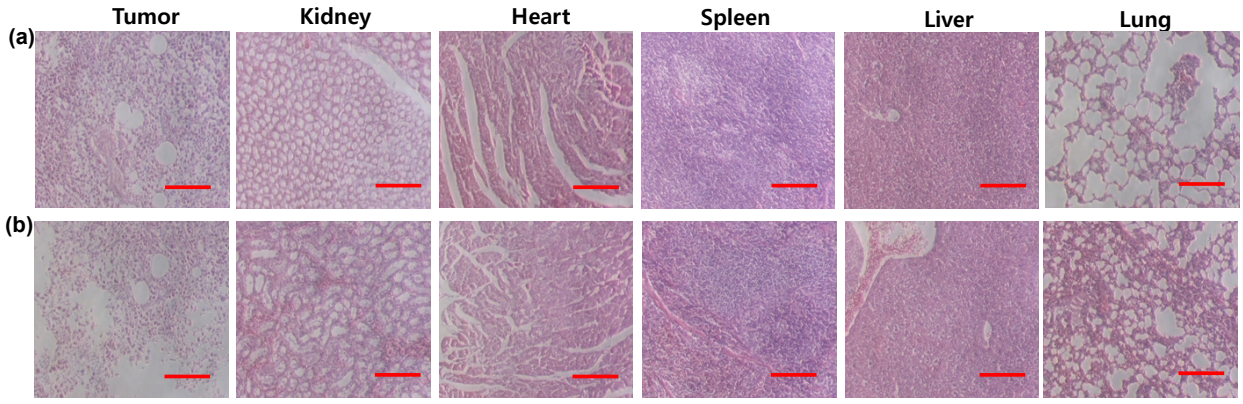

Fig. S9. Histological (H&E staining) observation of tissues of saline (a) and GDH nanogel (b) treated mice. Scale bar 100 μm.