File Name: Supplementary Information
Description: Supplementary Figures and Supplementary Tables

File Name: Peer Review File
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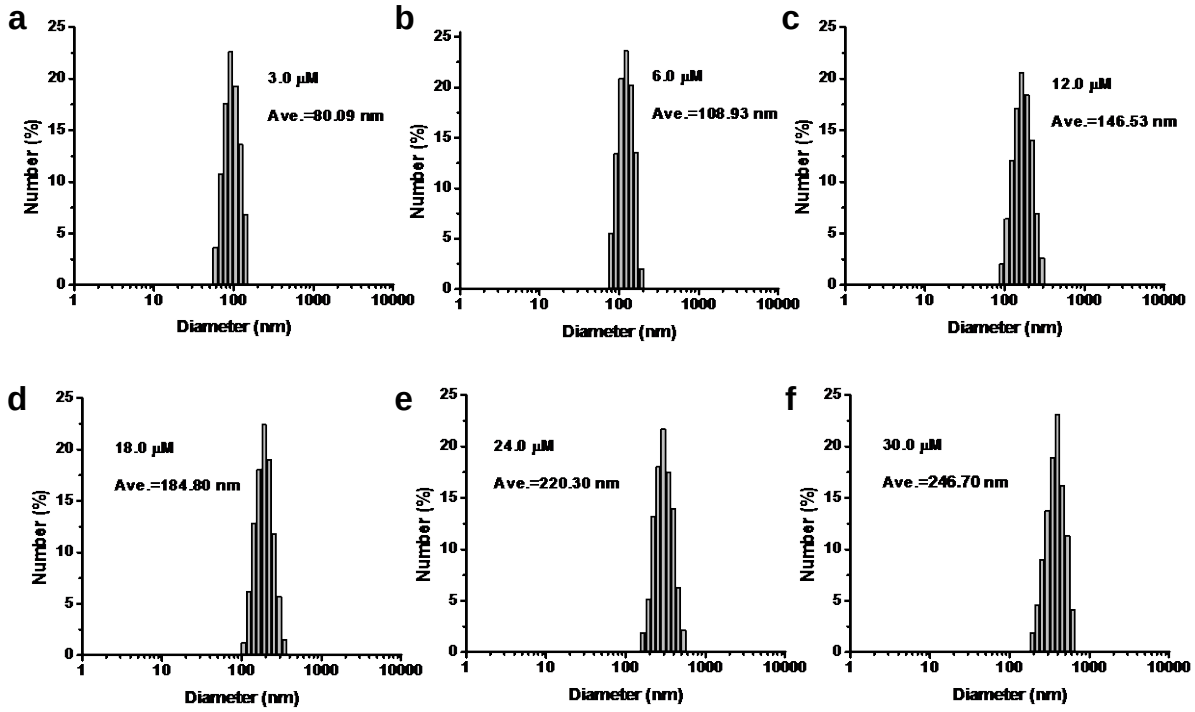
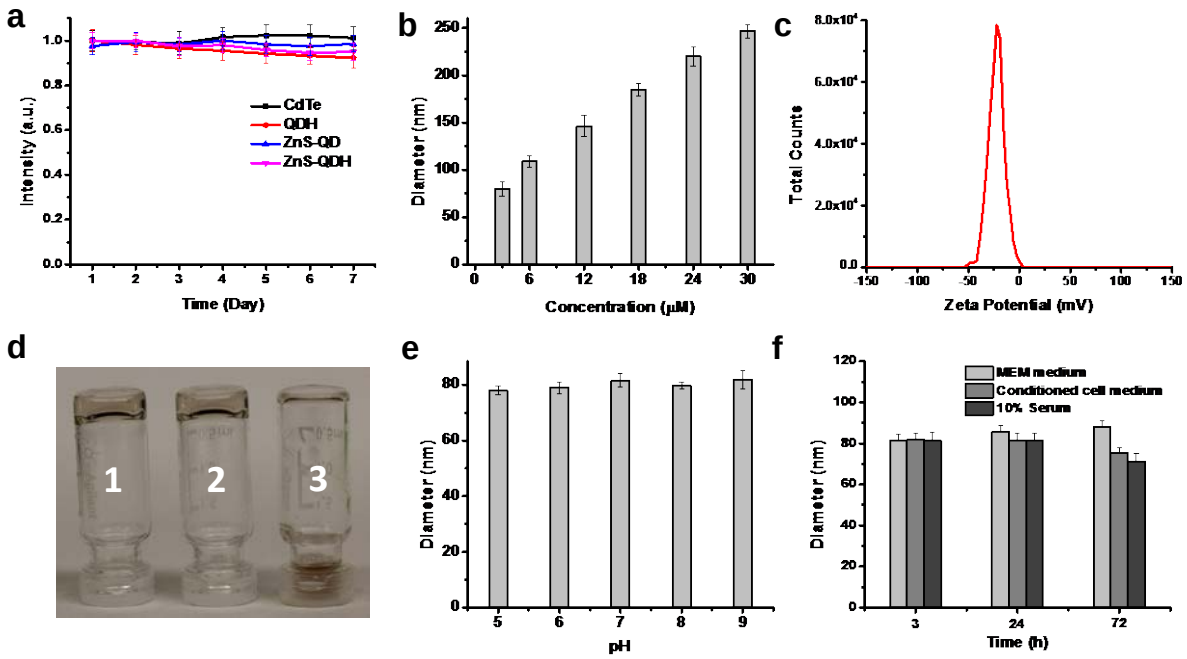
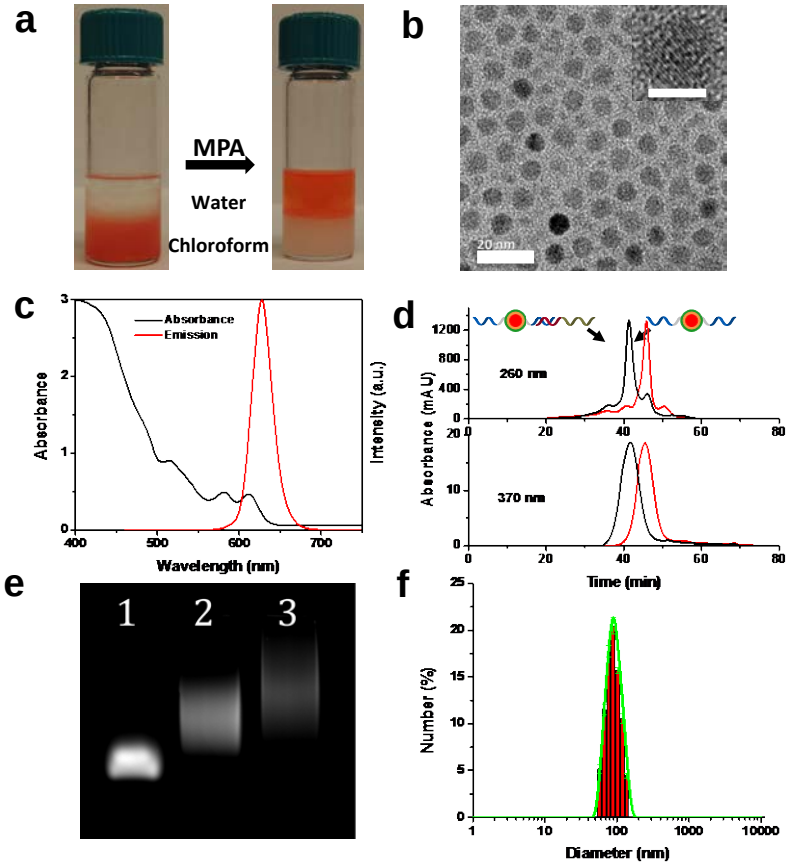


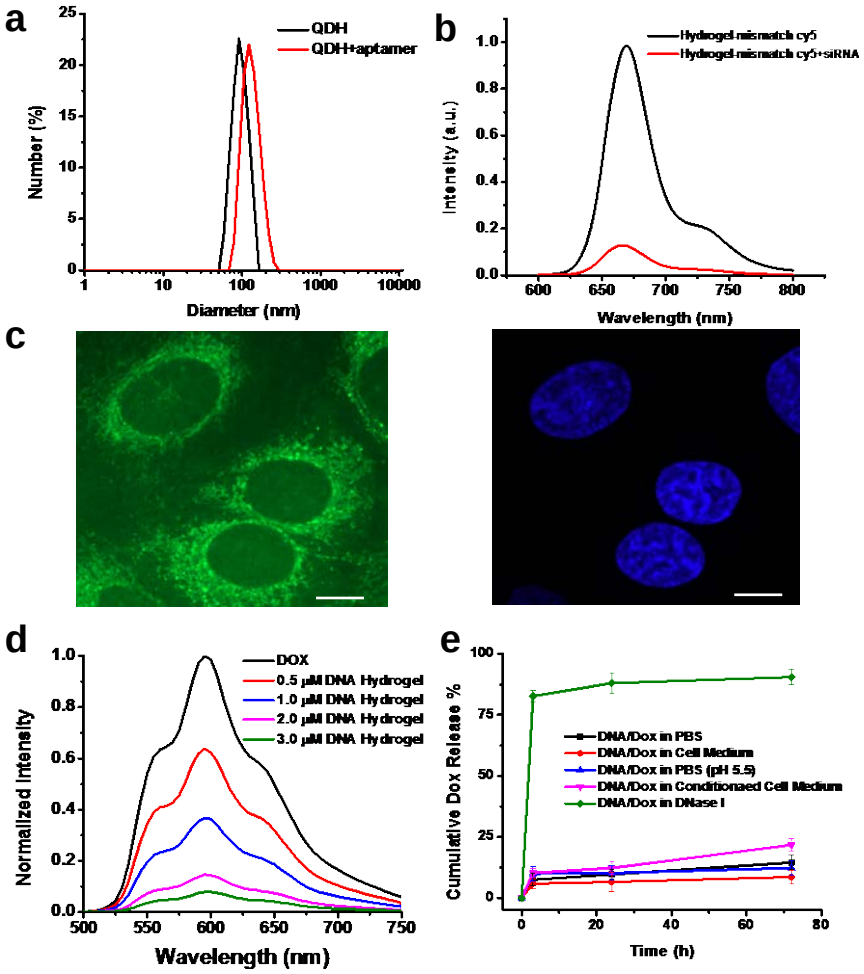

**Supplementary Figure 1. Hydrodynamic size of QDHs with different initial concentration.** Differential light scattering was used to estimate the size and dispersity of the QDHs.



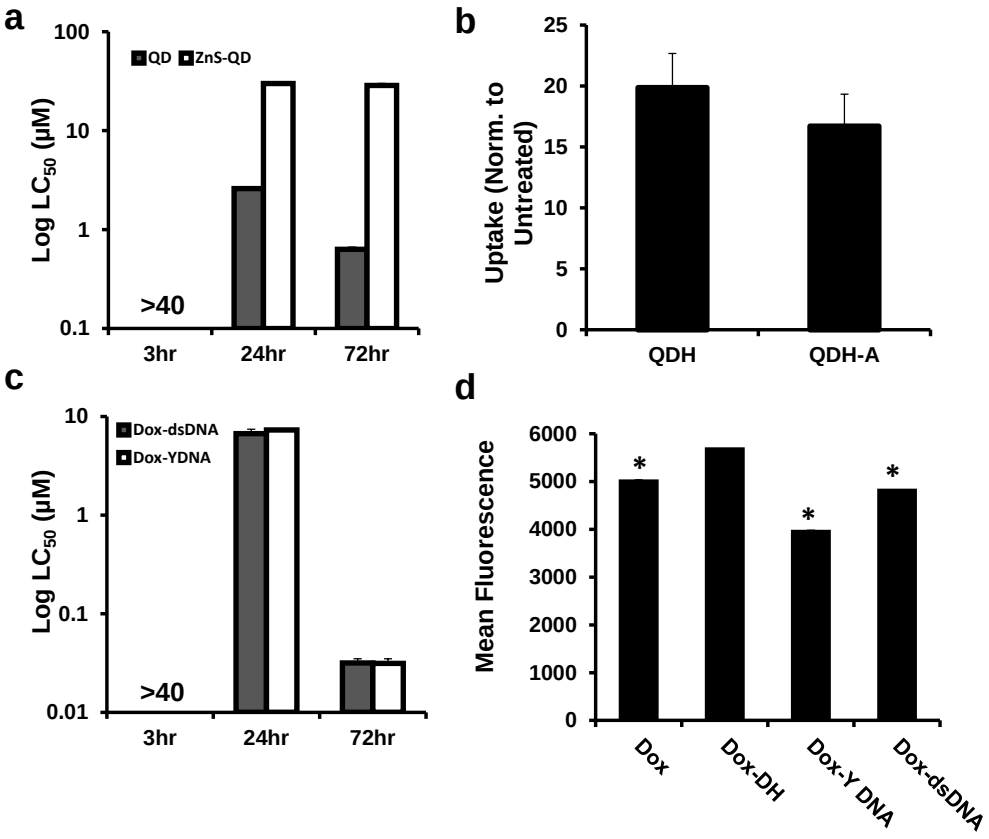

**Supplementary Figure 2. QDH characterization.** (**a**) The stability of the fluorescence intensity of QDs and QDH in different time. (**b**) Hydrodynamic size of QDHs with varying initial concentration. (**c**) Zeta potential of QDH analyzed by dynamic light scattering. (**d**) The temperature and enzymatic responsiveness of DNA hydrogels:(1) room temperature; (2) 37 °C for 3 h ;(3) DNase at 37 ° C for 3 h. Stabilities of QDHs monitored by luminescence and size changes at different pH after 72 h incubation (**e**) and different types of media over time (**f**). All error bars indicate s.e.m. (n=3).



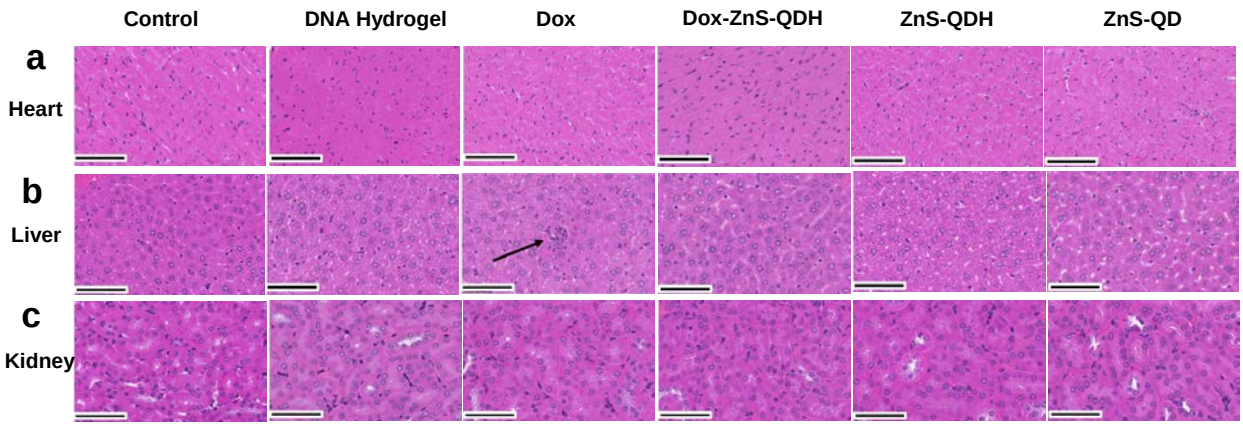

**Supplementary Figure 3. Characterization of CdSe/CdS/ZnS QDs.** (**a**) Red colored colloidal dispersion of CdSe/CdS/ZnS QDs undergoes the phase transfer from chloroform to water solution upon exchange of the original surface ligands with MPA. (**b**) TEM images of the CdSe/CdS/ZnS QDs (scale bars are 20 nm and 5 nm for low magnification and HRTEM images respectively). (**c**) Absorption and PL spectra of CdSe/CdS/ZnS QDs capped with MPA ligands dispersed in water solution. (**d**) High performance liquid chromatography characterization of CdSe/CdS/ZnS/DNA and the hybridization of template with complementary DNA. (**e**) Gel electrophoresis analysis of the binding of DNA to QD. Lane 1: QD; Lane 2: the mixture of QD and DNA; Lane 3, the mixture of QD and DNA with complementary DNA. (**f**) Hydrodynamic size of CdSe/CdS/ZnS/DNA hydrogels.



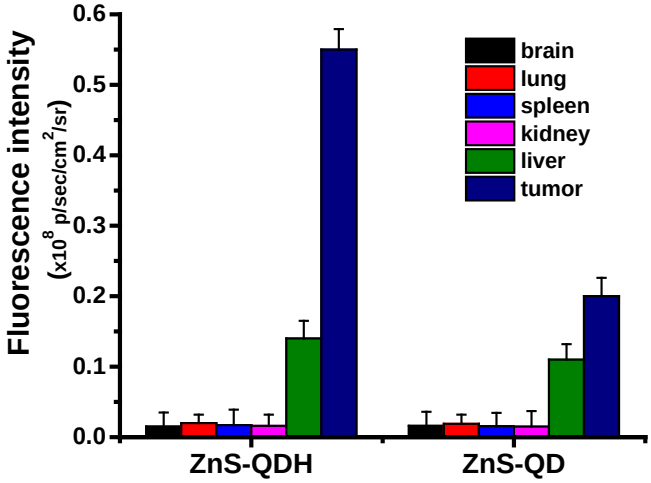

**Supplementary Figure 4. Aptamer-functionalized and Dox-loaded QDHs.** (**a**) Hydrodynamic size of QDHs and QDHs/aptamer. (**b**) The fluorescence intensity of before and after the competition reaction of siRNA with Cy5-labelled mismatched DNA to bind with QDHs. (**c**) Cellular accumulation of QDH-EGFR siRNA (green channel) in HeLa cells. Nuclei has been stained with Hoechst dye (blue channel). Scale bar is 5 microns. (**d**) Fluorescence spectra of Dox (50 μM) following incubation with increasing concentrations of DNA hydrogel (0-3 μM). (**e**) *In vitro* release profiles of Doxorubicin in different medium for different time at 37 °C. Error bars indicate s.e.m. (n=3).



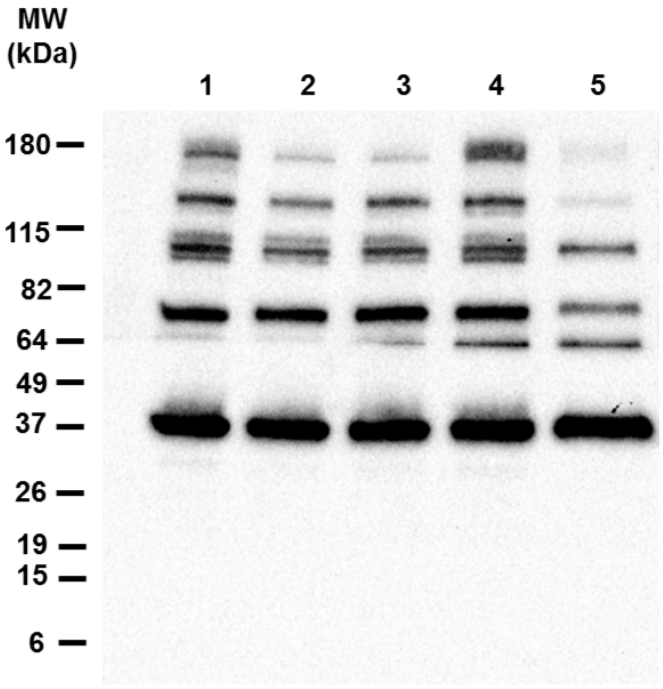

**Supplementary Figure 5. Cellular toxicity of QDH with and without Dox.** (**a**) Cell viability upon treatment with QD and ZnS-QD. (**b**) Measurement of cellular uptake of QDH and QDH-A in Ramos cells. (**c**) Cell viability of Dox-dsDNA and Dox-YDNA. (**d**) Comparison of potency of Dox, Dox-DH, Dox-YDNA, and Dox-dsDNA. All error bars indicate s.e.m. (n=3). One-way ANOVA vs. Dox-DH $p^* < 0.05$.




**Supplementary Figure 6. H&E staining of organs collected from treatment groups of healthy mice** (n=5 per group): (**a**) heart, (**b**) liver, and (**c**) kidney. Scale bar, 50 µm.




**Supplementary Figure 7. Quantification of fluorescence intensity of individual organs from ZnS-QDH and ZnS-QD treated mice.** All error bars indicate s.e.m. (n=5).




**Supplementary Figure 8. Full western blot corresponding to Figure 5b.** Approximate molecular weight (MW) of the protein ladder used is shown on the left side of the blot. EGFR band is depicted at ~ 175 kDa and GAPDH band at ~37 kDa. Note that the membrane (from the same gel) was cut in half to immunoblot for EGFR and GAPDH separately in their respective MW range.

**Supplementary Table 1.** Quantum yields for QDHs.

| Quantum Dots | Quantum Yield (%) |
|---|---|
| CdTe (Green) | 43.7 |
| CdTe (Yellow) | 35.6 |
| CdTe (Red) | 31.5 |
| CdSe/CdS/ZnS | 70.0 |

**Supplementary Table 2.** The swelling degree Q of the QDHs.

| Hydrogels (initial concentration) | Q (%) |
|---|---|
| 200 μM | 538.35 ± 30.24 |
| 100 μM | 341.69 ± 26.81 |
| 30 μM | 186.52 ± 24.17 |

**Supplementary Table 3.** DNA and RNA sequences

| Name | Sequence (5′ - 3′) (*indicate phosphorothioate linkage) |
|---|---|
| QD-DNA | GAGAGTCAATCGAAAAAAG*G*G*G*G*T*G*G*G*G*G*AAAAAAGAGAGTCAATCG |
| Y1 | CGATTGACTCTCGCTGTCCTAACCATGACCGTCG |
| Y2 | CGATTGACTCTCCGACGGTCATGTACTAGATCAG |
| Y3 | CGATTGACTCTCCTGATCTAGTAGTTAGGACAGC |
| Y1-2 | GCTGTCCTAACCATGACCGTCGCGATTGACTCTC |
| Y2-2 | CGACGGTCATGTACTAGATCAGCGATTGACTCTC |
| Y3-2 | CTGATCTAGTAGTTAGGACAGCCGATTGACTCTC |
| Aptamer | CGATTGACTCTCAAAAAATCTAACTGCTGCGCCGCCGGGAAAATACTGTACGGTTAGA |
| mis-cy5 | Cy5-CGAGTGACTATC |
| siRNA sense | rGrCrArArArGrUrGrUrGrUrArArCrGrGrArArUrArGrGrUrArU |
| siRNA antisense | RArUrArCrCrUrArUrUrCrCrGrUrUrArCrArCrArCrArCrUrUrUrGrCAAAAATAAAAATAAAAA CGATTGACTCTC |
| dsDNA | CGATTGACTCTCGCTGTCCTAACCATGACCGTCGCTGATCTAGTAGCAGC |
| | GCTGCTACTAGATCAGCGACGGTCATGGTTAGGACAGCGAGAGTCAATCG |