Supporting information for:

Assessing Clinical Prospects of Silicon Quantum Dots: Studies in Mice and Monkeys

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Figure S1 shows that levels of biochemistry markers and blood cell counts of rhesus macaques are similar to those of human. The bars for the monkey values appear directly above the human values. The plots indicated that most monkey and human parameters are within a reasonable range when compared to one another. We believe this makes rhesus macaque suitable for primate evaluation of nanoparticles. We monitor the weight, behavior and blood chemistry parameters to gain insight into the impact of silicon nanocrystals on primates after intravenous injection.

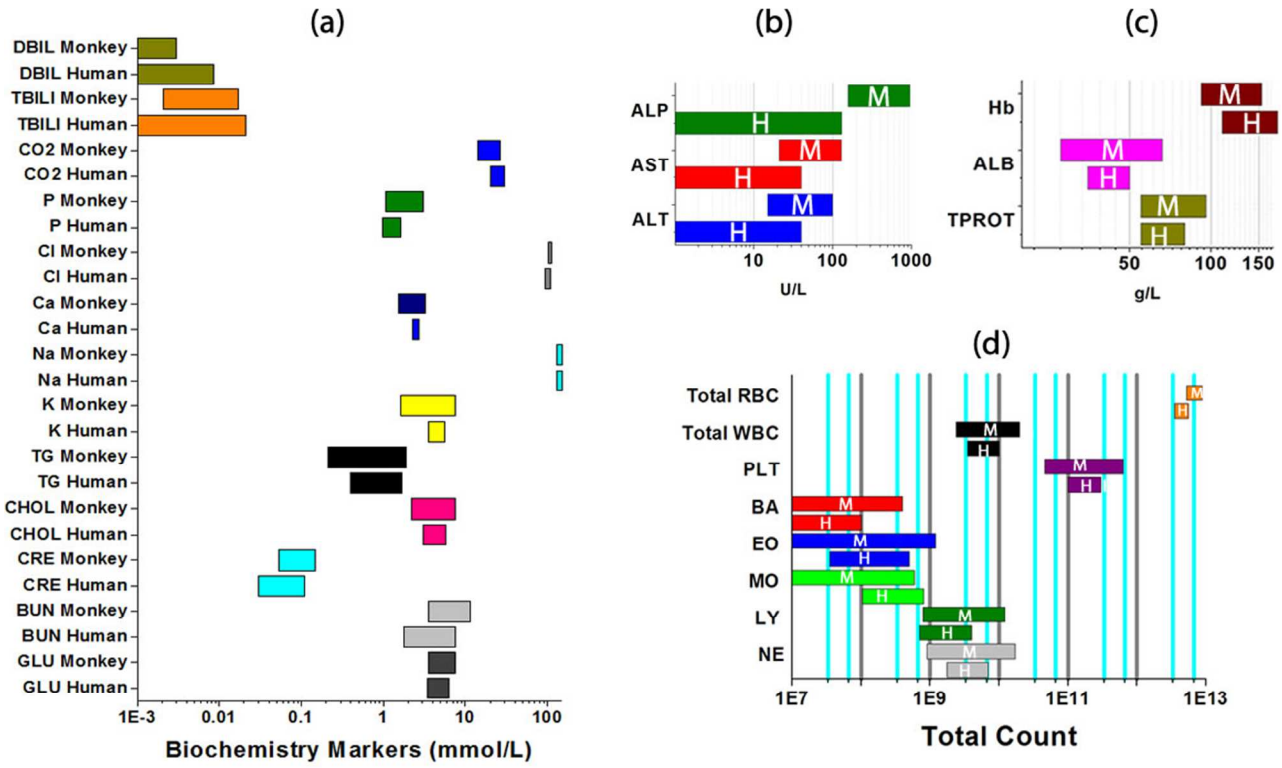

Figure S1. Plots show that biochemistry markers and blood cell counts of monkeys are similar to those of human[1]. The normal ranges for the biochemistry parameters for rhesus macaques are directly above those for humans. Panel (a) shows biochemistry markers with units of mmol/L. Panel (b) shows parameters with Units per liter, Panel (c) shows biochemistry parameters with g/L and panel (d) shows the total counts of red blood cells, platelets and white blood cells.

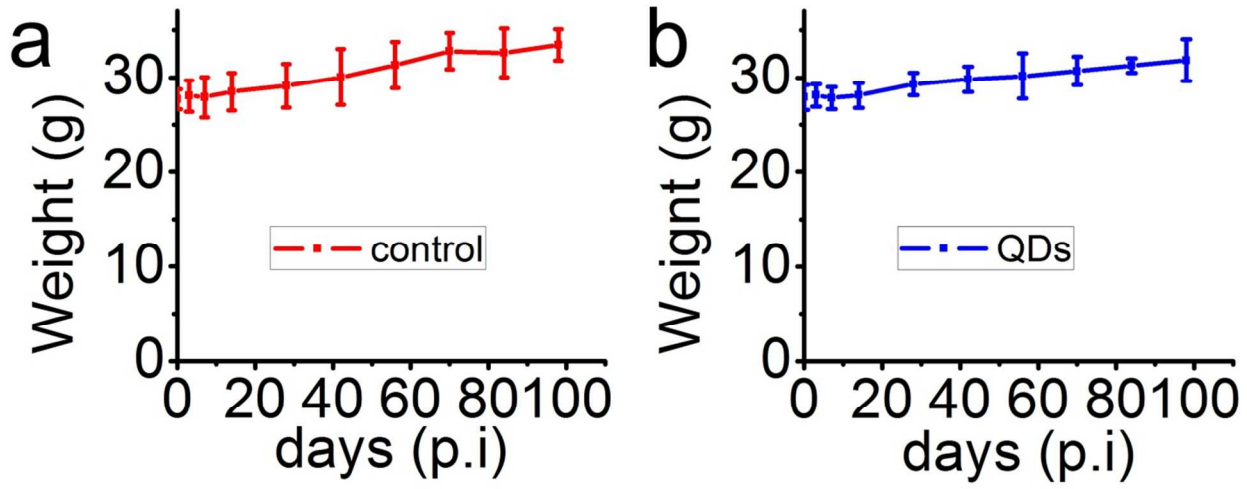

Figure S2. Body mass of mice (n=5) over the course of the study. Figure a is the body mass of the uninjected mice (n=5) plotted against time. Figure b is the body mass of the mice (n=5) injected with SiQDs plotted against time.

Table S1.Difference between silica and silicon

Silica nanostructures	Silicon nanocrystals
Molecular Formula – SiO_2	Molecular Formula - Si
Used to encapsulate active materials e.g gold	Used as Active Material e.g. optical imaging
Amorphous	Crystalline
Non-Luminescent	Luminescent
Well studied	New and novel material
Generally used as a controllable coating	Never used as coating
Never used for size controlled emission	Used for size-tunable emission

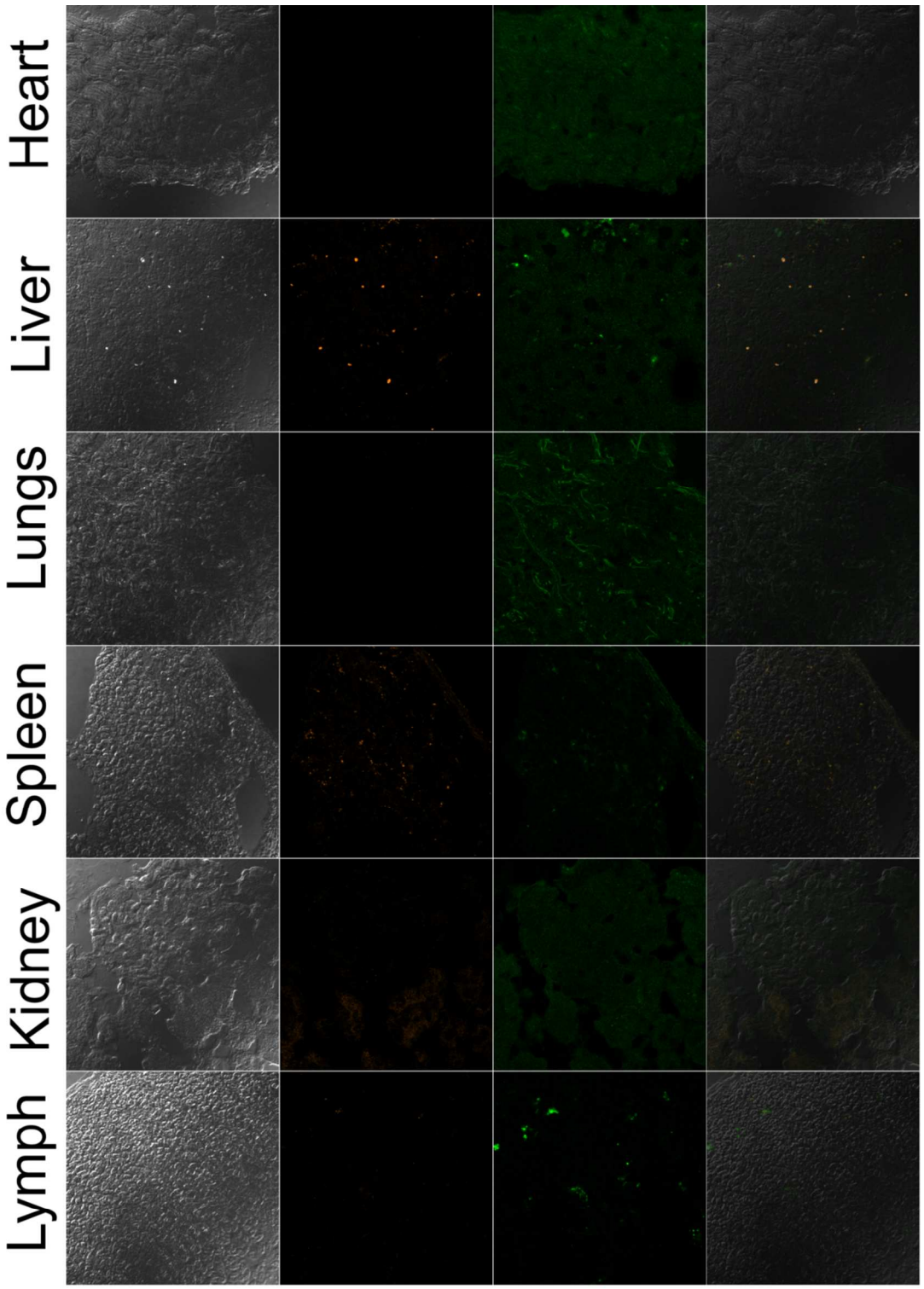

Figure S3. Confocal imaging signal of silicon quantum dots in tissue sections from mice 3 days post treatment. Images with the transmission, fluorescence from Si QD, fluorescence from tissue, and overlaid images are shown from left to right.

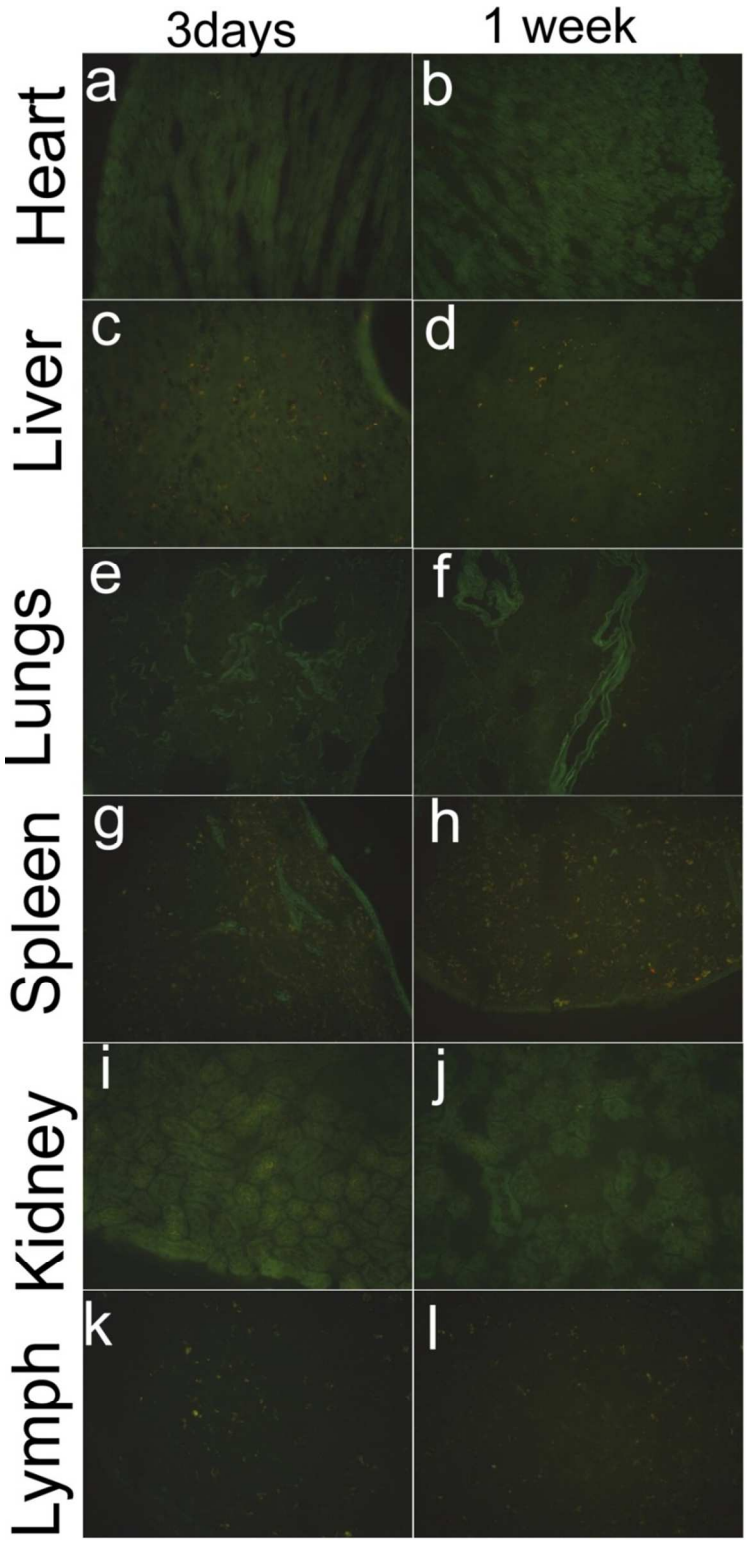

Figure S4. Fluorescence imaging of frozen tissue sections from mice 3 days and 1 week after injection with micelle encapsulated silicon quantum dots. In all cases, green represents emission from the tissue and red represents emission from Si QDs.

H & E staining analysis.

H & E stained sections were analyzed by a clinical pathologist, who reported the following. For untreated controls (0 days): Normal hepatic lobule structure; No cloudy swelling in hepatocyte; No steatosis in hepatocyte; No necrosis observed; No cholestasis; No proliferation of kupffer cells. For mice 3 days post injection: Normal hepatic lobule structure; No cloudy swelling in hepatocyte; No steatosis in hepatocyte; No cholestasis; Spotty necrosis observed; Proliferation of kupffer cells observed; Inflammatory cell infiltration observed. For mice 1 week post injection: Normal hepatic lobule structure; No cloudy swelling in hepatocyte; No steatosis in hepatocyte; No cholestasis; Spotty necrosis observed; Proliferation of kupffer cells observed; Inflammatory cell infiltration observed. For mice 6 weeks post injection: Normal hepatic lobule structure; Cloudy swelling in hepatocyte observed; No steatosis in hepatocyte; Spotty cholestasis observed; Spotty necrosis observed; Proliferation of kupffer cells observed; Inflammatory cell infiltration observed. For mice 14 weeks post injection: Normal hepatic lobule structure; confluent cloudy swelling in hepatocyte observed; No steatosis in hepatocyte; Multifocal cholestasis observed; Spotty necrosis observed; Proliferation of kupffer cells observed; Inflammatory cell infiltration observed; For control mice that were not injected with nanoparticles (14 weeks): Normal hepatic lobule structure; No cloudy swelling in hepatocyte; No steatosis in hepatocyte; No necrosis observed; No cholestasis; No proliferation of kupffer cells. The apparent response to the silicon QD formulation was delayed and increased with time. The observed effects may be caused by the silicon or by other agents in the nanocarrier. The persistence of the particles in the liver may contribute to the inflammation, proliferation of kupffer cells, multifocal cholestasis and spotty necrosis of hepatic cells observed by the pathologist.

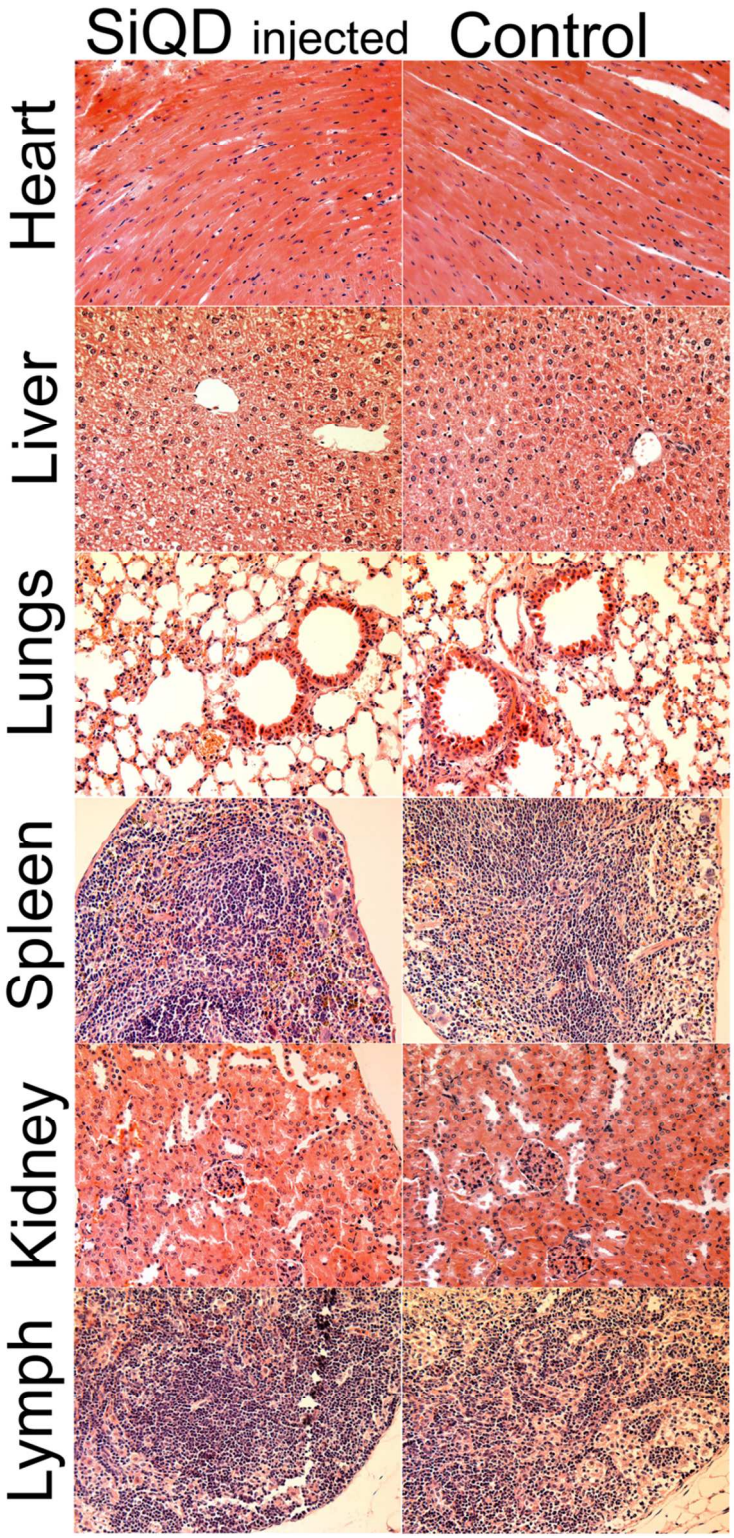

Figure S5. Histological images in mice after 14 weeks. Tissues were harvested from the heart, liver, spleen, lung, kidney, and lymph.

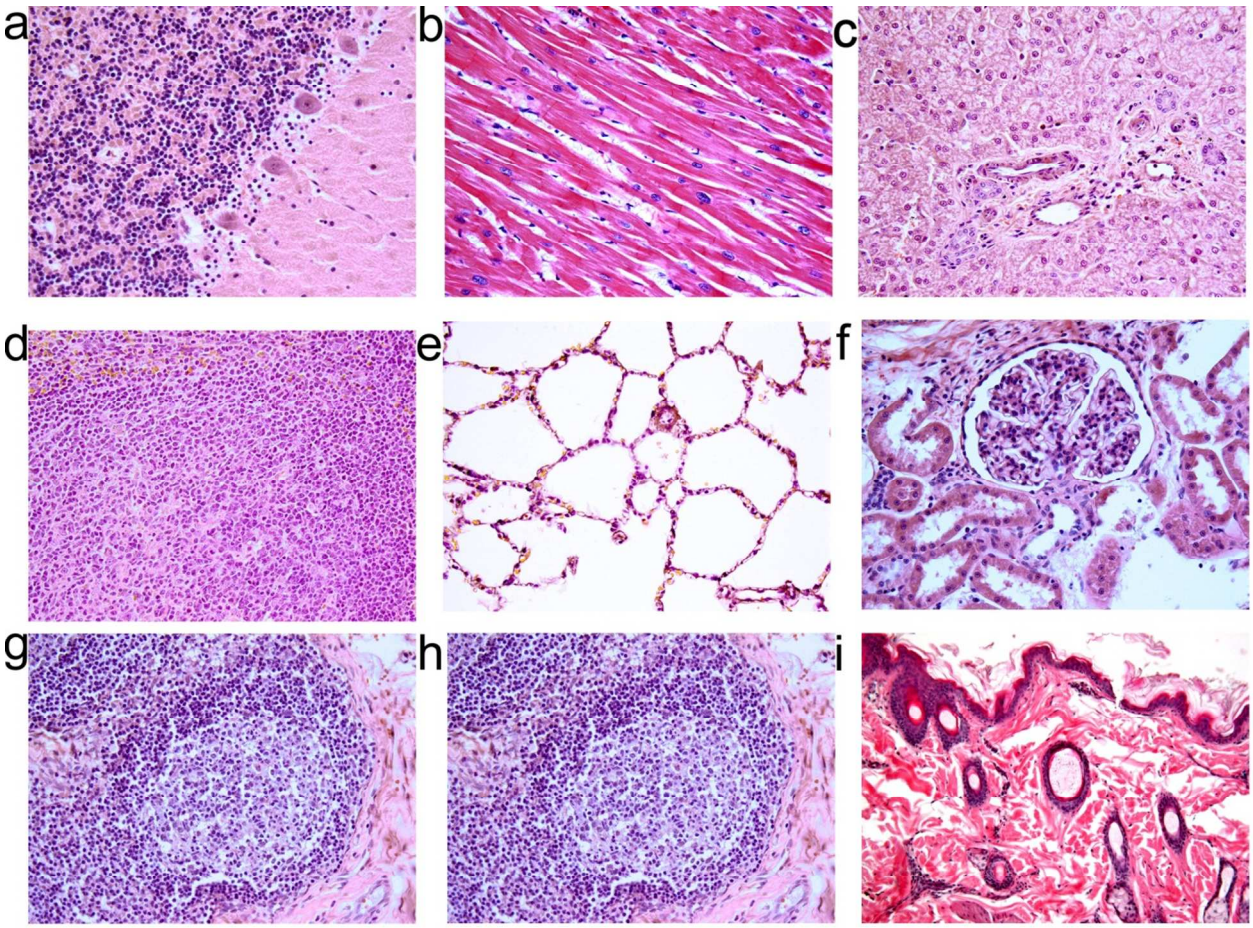

Figure S6. Histological images in 2nd rhesus macaque reveal no signs of silicon nanoparticle induced toxicity after three months. No anomalies were observed in the tissues. Tissues were harvested from (a) brain, (b) heart, (c) liver, (d) spleen, (e) lung, (f) kidney, (g) lymph, (h) intestine, and (i) skin. The images were taken at 40x magnification.

1. Ye, L.; Yong, K.-T.; Liu, L.; Roy, I.; Hu, R.; Zhu, J.; Cai, H.; Law, W.-C.; Liu, J.; Wang, K. *et al.* A Pilot Study in Non-Human Primates Shows No Adverse Response to Intravenous Injection of Quantum Dots. *Nat Nano* **2012,** *7*, 453-458.