Supplementary Information (ESI)

Table S1. The drug entrapment efficiency (DEE) and drug loading content for PU NPs encapsulating different amounts of VK3. We observed that VK3 could be loaded to a higher amount (4.83%). This was about a 15-fold increase (vs. 0.33%), though the value of DEE decreased from 97% to ~74%.

Amount of VK3 (g) added in 15.31 g of PU during preparation	**0.05**	**1**
Drug entrapment efficiency (DEE, %)	97.01 ± 0.19	73.86 ± 2.05
Drug loading content (%)	0.33	4.83

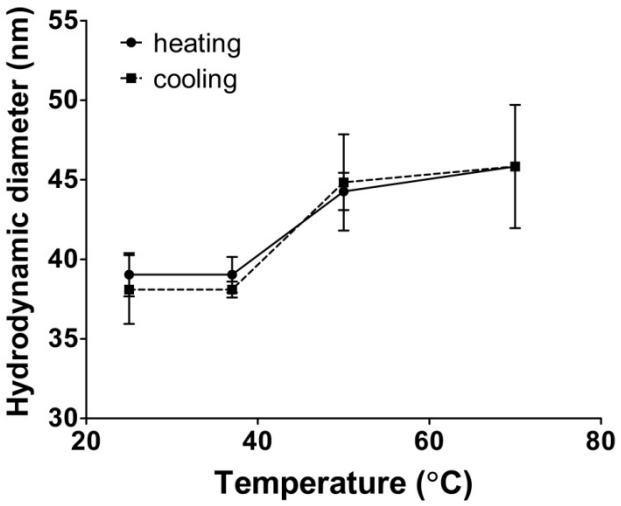

Figure S1. The hydrodynamic diameter changes of PU NPs at 25, 37, 50, and 70°C measured by DLS using the submicron particle analyzer. The data at 70°C may be less accurate because of water bubbles appearing at this temperature. The temperature where the size of NPs started to increase was near the softening temperature (50–60°C) of PCL diol used for PU synthesis. Moreover, the temperature-responsive change in hydrodynamic diameter was reversible upon heating and cooling.

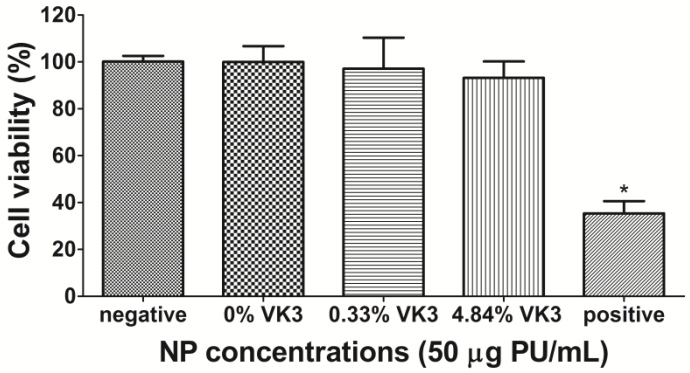

Figure S2. The cytoxicity of PU NPs of (50 μg PU/mL) loaded with different amounts of VK3 on HepG2. Negative and positive controls were the culture medium (without any NPs) and that containing dimethyl sulfoxide (DMSO, 5%), respectively. *$p < 0.05$ with respect to the negative control (0 μg PU/mL). The data indicated that VK3-PU NPs had no cytoxicity to HepG2.

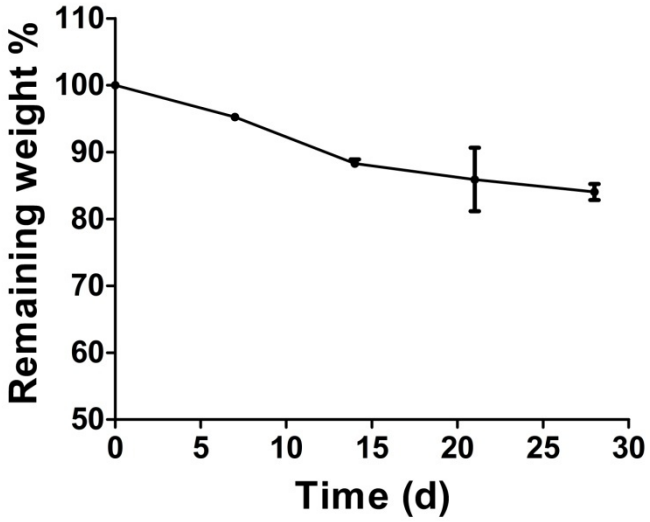

Figure S3. The degradation profile of PU (5 mm×5 mm film) in PBS (pH=7.4, at 50°C). About 15% PU was degraded in a month. It was thus apparent that our PU was biodegradable.

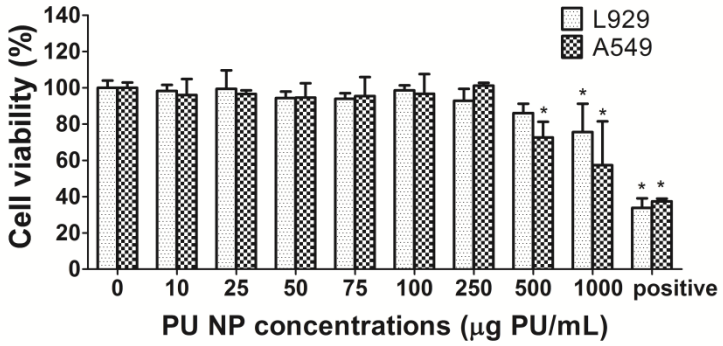

Figure S4. The cytoxicity of PU NPs for a normal healthy cell line (L929 skin fibroblasts) and a lung cancer cell line (A549 human lung carcinoma epithelial cells). The positive control was the culture medium containing 5% DMSO. The negative control was 0 μg PU/mL. *$p < 0.05$ with respect to 0 μg PU/mL. These data suggest the pristine PU NPs had no cytoxicity at concentrations below 250-500 μg PU/mL.

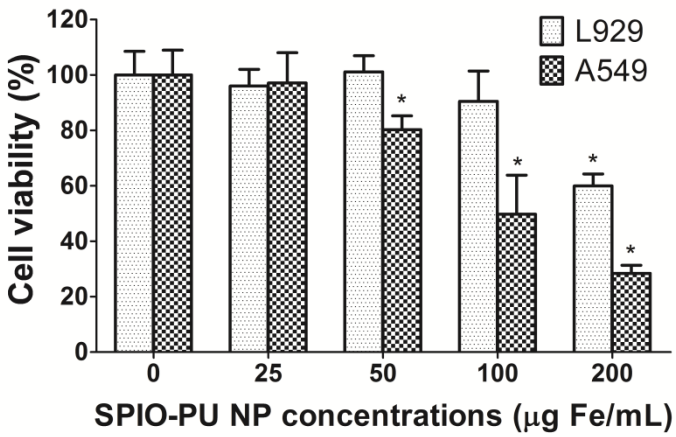

Figure S5. The cytoxicity of SPIO-PU NPs on the normal healthy cell line (L929) and a lung cancer cell line (A549). *$p < 0.05$ with respect to 0 μg Fe/mL. Results indicated that SPIO-PU NPs were not cytotoxic to L929 fibroblasts below 100 μg Fe/mL. On the other hand, A549 lung cancer cells (and HepG2 hepatoma cells in the main text) were more susceptible to SPIO-PU NPs.

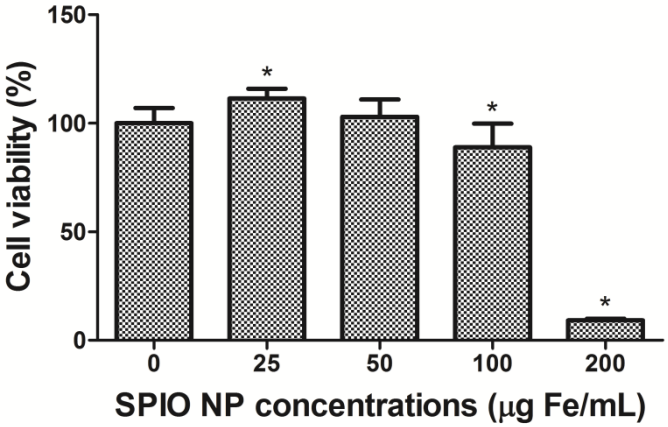

Figure S6. The cytoxicity of sodium oleate-stabilized SPIO NPs to L929 fibroblasts.*$p < 0.05$ with respect to 0 μg Fe/mL. The data suggested that oleate-SPIO NPs up to 50 μg Fe/mL were not toxic to L929 fibroblasts. Besides, our SPIO-PU NPs were not more cytotoxic than the oleate-SPIO NPs for the normal cell line.

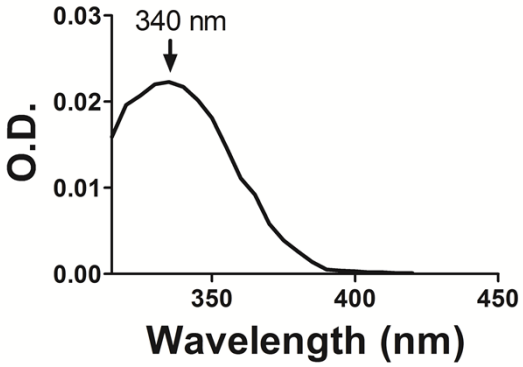

Figure S7. Typical absorption of VK3 detected for SPIO-VK3-PU NPs. SPIO-VK3-PU NPs were purified by magnetic separation. To confirm that SPIO and VK3 were both encapsulated in PU NPs, VK3 was extracted by ethanol, removed of SPIO at 7000 rpm, and separated by a 50 kDa centrifugal ultrafilter. The typical optical absorption of VK3 (340 nm) was clearly detected in the extract. This supported that SPIO and VK3 were both encapsulated in PU NPs.