SUPPLEMENTARY MATERIAL

Activation of CYP3A by ABC phenomenon potentiates the hepatocellular carcinoma-targeting therapeutic effects of PEGylated anticancer prodrug liposomes

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ABC phenomenon potentiates anti-HCC efficacy

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**Supplemental Figures:**

**Supplemental Figure 1.** Characterization of PEG-DiR-L. (A) Photograph of PEG-DiR-L solution. (B) Morphology of PEG-DiR-L measured by a transmission electron microscope (TEM). Scale bar represents 100 nm. (C) Size distribution PEG-DiR-L measured by photon correlation spectroscopy (PCS, mean ± SD, n = 3).

**Supplemental Figure 2.** Verification of HCC rat model. (A) Photographs and pathologic staining
of liver tissue from normal and model rats. (B) Line graphs of body weight changes during modeling in normal and model rats. (C) Liver function indices and hepatocellular carcinoma-specific indices in normal and model rats. Data are expressed as mean ± SD (n = 10, ***P < 0.001).

**Supplemental Figure 3.** (A) **Ex vivo** imaging at 6 h after injection of HCC mice injected with DiR (mean ± SD, n = 3). (B) **Ex vivo** imaging at 6 h and 12 h after injection of HCC mice repeatedly injected with PEG-L at different time points (mean ± SD, n = 3).
**Supplemental Figure 4.** Toxicity to tissues of other organs by repeated injection administration. Histopathologic staining results of the heart, spleen, lungs, and kidneys. (mean ± SD, n = 7).

**Supplemental Figure 5.** (A) Effect of CYP3A enzyme inhibitors on the concentration and (B) relative concentration of splenic CP administered by repeated injections of PEG-L (mean ± SD, n = 3, ***P < 0.001).